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Original Communications

THE SURGICAL TREATMENT OF MITRAL STENOSIS

II. PROGRESS IN DEVELOPING A CONTROLLED VALVULOPLASTIC TECHNIQUE

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THE background of the surgery of mitral stenosis has been reviewed in a previous communication.[1] The earlier thinking and the earlier experiences[2-18] reduced the problem to a consideration of the relative significance of mitral stenosis versus regurgitation. There is now evidence that there are various types of regurgitation, some borne much better than others.

The correction of mitral stenosis is no longer directed at the production of insufficiency but at reducing the stenotic block with the greatest possible restoration of valvular function. While much previous work has been based on the concept of exchanging regurgitation for stenosis, it does not follow that this is either desirable or necessary.

At the present time there is no method of determining quantitatively the degree of regurgitation or of stenosis in a given patient. Since stenosis and regurgitation may affect the pulmonary and cardiac dynamics differently, the choice of operation would be greatly influenced by knowledge of these factors. In gaining such specific knowledge and in evaluating the general cardiovascular status it is highly desirable to apply as many objective tests as possible. At present, these objective tests must include cardiac catheterization for the determination of blood flow and intracardiac and pulmonary vascular pressures.

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The medical evaluation of patients and cardiac catheterization studies were carried out at the Thorndike Memorial Laboratory, Second and Fourth Medical Services (Harvard), Boston City Hospital; the Cardiovascular Laboratory, Peter Bent Brigham Hospital; and the Department of Medicine, Harvard Medical School.

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CLASSIFICATION OF PATIENTS WITH RESPECT TO SURGICAL PROCEDURES

In previous communications a preliminary classification of patients with mitral stenosis was offered with respect to their suitability for different operations. This classification has undergone modification, but the original outline follows:

Group A includes patients with a *low resting cardiac output* which increased little or not at all on exercise. Right ventricular failure may or may not have been present. For such patients, the operation of "valvuloplasty" may be helpful since, in these individuals, mitral obstruction is of major importance in their clinical condition.

Group B comprises patients with *normal resting cardiac outputs* that usually increase with exercise. The pulmonary symptoms may be as severe as in the patients in the first group. In these persons mitral regurgitation rather than stenosis may be the predominant factor, or the cardiac output may be maintained only by a high left auricular pressure driving blood through the stenotic mitral valve. For these patients, a beneficial though purely palliative procedure is the surgical production of an interatrial septal defect or the ingenious azygos to pulmonary vein shunt used by Sweet and Bland[19] to decompress the left auricle and the pulmonary venous hypertension, especially at high peaks during periods of strain. Such operations would not be suitable for patients who have had right ventricular failure because the recirculation of blood through this chamber and the pulmonary circulation would place an added burden on the right ventricle. This procedure would also be contraindicated in patients with a low resting cardiac output; in them, too great a proportion of blood might be diverted through the shunt, and the left auricular pressure might be so lowered that the blood flow through the mitral orifice to the periphery would be insufficient to sustain life.

Group C includes patients whose incapacitating symptoms, particularly attacks of pulmonary edema, are associated with *rapid heart action* that cannot be controlled by medical measures. The cardiac output may be normal or low, and the pulmonary artery pressure is always elevated. The patients are not deemed suitable candidates for either of the operations just mentioned because of the severity of their disease. The occasional patient with mitral stenosis who has attacks of severe chest pain, so-called "hypercyanotic angina," may also fall into this group.[20] For these patients, a palliative procedure may be the removal of the cardiac sympathetic accelerator and afferent nerves. In two successive operations, the inferior cervical ganglion and the first four or five dorsal sympathetic ganglions are removed from each side through a small cervical incision. The relief afforded is through the production of a slower heart rate or the interruption of pain fibers. It is also possible that some additional direct effect on the pulmonary circulation is produced.

With increase in our knowledge, gained from operative experience and study of a group of twenty-five patients by cardiac catheterization and other

methods, we have modified this classification. It has become apparent by observation of four cases confirmed at operation or autopsy that *high grade mitral stenosis can exist* in patients whose *resting cardiac output* is normal as determined by catheterization. It is quite probable that this resting output is close to the maximum that can be attained. Therefore, definite clinical improvement may take place in patients following the vulvuloplastic operation, with significant lowering of the pulmonary arterial pressure, yet with no change in the level of the resting cardiac output. It is evident, therefore, that too much reliance cannot be placed on the cardiac output alone as a guide to operability. There may be functional and structural alterations in the heart and in the pulmonary circulation. Marked diminution of the stroke volume and still further elevation of the pulmonary vascular pressure may be coincident with the tachycardia of exercise or anxiety.

In the present experimental stage of the procedure, the operations under discussion should be considered only in patients with uncomplicated mitral valve disease in whom there is no evidence of a significant degree of involvement of other valves, of the myocardium itself, or of associated disease.

SOME FUNDAMENTAL PRINCIPLES OF MITRAL VALVULOPLASTIC SURGERY

Four surgical principles pertaining to mitral valvuloplasty have been presented[1]:

I. The operation should be performed without dislocation of the heart from position of optimum function.

II. The buttonhole opening of the stenotic mitral valve should be approached from the auricular side so that the funnel directs the cutting instrument toward the leaflet margin.

III. Surgical enlargement of the stenotic orifice should be so planned that there is a minimum burden from associated regurgitation (''selective insufficiency'') and maximum restoration of valvular function (''valvuloplasty'') (Fig. 1).

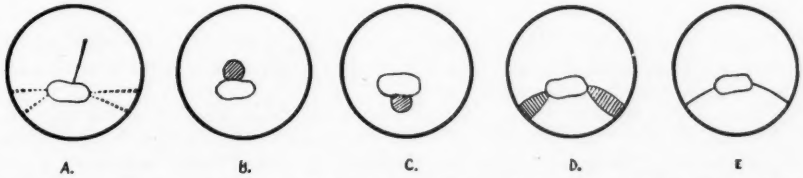

Fig. 1.—Diagrammatic representation of various operations in the stenotic mitral ring as seen from above. *A*, Anterior valvulotomy (dotted lines indicate zones in the solid stenotic funnel that were commissures in the predisease state); *B*, anterior leaflet insufficiency; *C*, posterior leaflet insufficiency—"selective insufficiency"; *D*, "selective insufficiency" and "valvuloplasty" by excision of the immobilizing commissure bridges; *E*, "valvuloplasty" by incision in the zones of the commissures.

IV. In the presence of mitral obstruction or regurgitation, undue acceleration of the heart rate must be avoided. This acceleration is avoided by eliminating all possible ordinary sources of tachycardia incident to surgery, by adequate digitalization, and by the use of intravenous procaine at the time of

operation to reduce cardiac irritability. Tachycardia increases pulmonary vascular pressure and is associated with pulmonary edema and other forms of "pulmonary decompensation."

Now we may add two more principles and clarify further some of the previous statements through experience with three new valvuloplasty patients. These case presentations will show that:

V. Blind intracardiac maneuvers must be well controlled and deliberate.

VI. There must be the least possible stimulation of the ventricular endocardium during intracardiac operation.

In this field of surgery, the experimental animal is of only partial help. Each new human problem must be approached with care and the maximum experience gained from each surgical operation. Our intracardiac manipulations have been not only blind, but hurried and ill controlled. It would not be so hazardous to work quickly if we could see well, directly or indirectly. An adequate cardioscope is, unfortunately, not yet available.[11, 15, 21] Quite naturally, we look forward to the satisfactory extracorporeal pump that will allow deliberate open intracardiac surgery. Björk in Crafoord's laboratory,[22] Gibbon,[23] and Jongbloed[24] have gone far but they have not yet offered a pump suitable for human use.

It would not be such a handicap to work blindly if one could be deliberate and carefully palpate for the stenotic opening with suitable instruments, could map the pattern of the rolled "fishmouth," and could then deliberately incise or resect the fused commissures, and excise suitable portions of the posterior leaflet. This should be controlled by frequent auricular and ventricular pressure recordings.

Four new operative experiences with valvuloplasty are presented here because they illustrate (a) the need for more deliberate cardiac manipulation, (b) the need for better control of the open auricle and consequent loss of blood, (c) the need for frequent pressure soundings as a guide to the pattern and extent of excision, and (d) the steps taken to meet these needs.

CASE REPORTS

Mitral Stenosis Case 6, Valvuloplasty No. 3.—F. M., a 32-year-old housewife, was referred to the U. S. Naval Hospital, Chelsea, Mass. on Dec. 12, 1948, with the chief complaint of increasing dyspnea for the past seven years.

Seven years previously, during her only pregnancy, a heart murmur was discovered and digitalis was begun. Four years prior to admission, there was an aggravation of symptoms of dyspnea, cough, and frothy sputum. Digitalis was discontinued because of nausea. One year prior to this admission, the patient had an episode of severe cough accompanied by a large quantity of blood-tinged, frothy sputum which was diagnosed as "inter-lobar pleurisy" and subsided with conservative therapy. During the past year, dyspnea, weakness, and marked palpitation of the heart became more distressing. The patient had to restrict her activities greatly. She walked little and had to be carried upstairs. Digitalis was begun again. There has never been any peripheral edema.

The past history revealed no definite history of rheumatic fever. The patient had two attacks of diphtheria about eleven years prior to admission.

Physical examination revealed a pale, thin, rather underdeveloped woman. General physical examination was not remarkable except for the cardiovascular system. The maximal apical impulse was 9 cm. to the left of the midsternal line in the fifth interspace and the

left border of dullness was percussed at 10 cm., 3 cm. beyond the midclavicular line. There was an apical diastolic thrill. The first mitral sound was snapping in quality. There was a Grade II apical systolic and a low-pitched Grade III diastolic rumble with presystolic accentuation as well as a Grade I high-pitched early diastolic murmur in the pulmonic area. The rhythm was regular with a resting rate of 88 that rose to 140 on mild exercise. The lungs were clear. There was no venous congestion, hepatomegaly, ascites, or peripheral congestion. Blood pressure was 120/80.

Teleroentgenography showed a 25 per cent enlargement in the transverse diameter of the heart, and marked prominence of the pulmonary conus with evidence of left auricular enlargement in the oblique view. The electrocardiogram was consistent with right ventricular and auricular enlargement. The venous pressure was 95 to 110 mm. of water, and rose to 140 with hepatic pressure. Blood examination on admission revealed the hemoglobin to be 11 Gm., the red count to be 4,540,000 and hematocrit 41.

Preoperative catheterization studies are shown in Table I.

Mitral valvuloplasty was done Jan. 6, 1949. Premedication was Seconal 100 mg., scopolamine 0.65 mg. Anesthesia was brief pentothal induction, then endotracheal ether.

Electrocardiographic tracings were followed throughout the procedure by medical consultants.

Incision was made from the second rib on the left immediately lateral to the sternum in the inframammary line to the midaxilla. During the opening of the chest wall, electrocardiograms revealed idioventricular rhythm and irregular runs of auricular fibrillation. Extrasystoles and ventricular tachycardia were noted, and on three occasions over a period of thirty minutes, 20 c.c. of 1 per cent procaine were administered intravenously. After reflecting the left breast upward, the incision was carried through the left third interspace from the sternum to the midaxillary line. The mammary vessels were ligated proximally and distally, then divided. As the ribs were exposed, the third and fourth costal cartilages were divided 1.5 cm. to the left of the sternum. Irregularity of beat was accentuated with the spreading of the ribs. The pericardium was opened over the left auricular appendage in a linear fashion 1.5 cm. anterior to the left phrenic nerve, and No. 2 braided silk stay sutures were placed for exposure. As one stay suture was inserted, the auricular appendage was inadvertently nicked, but bleeding was controlled with a small snap.

A 000 black Deknatel suture was inserted in purse-string fashion about the tip of the left auricular appendage and a No. 2 black silk braided suture was set, but not tied at the base of the appendage. At this point in the operation the patient's blood pressure became imperceptible and there was dilatation of the ventricles with runs of ventricular tachycardia, followed by slow idioventricular rhythm and then fibrillation. The heart appeared to be motionless. Manual massage of the heart was instituted. This cardiac massage was carried out by the surgeon (D. E. H.) who placed his left hand palm upward on the phrenic surface of the heart, meanwhile supporting the dilated exposed anterior surface of the heart with the cupped palm of the right hand. After approximately eight minutes, the heart appeared to fibrillate. Throughout this period of apparent arrest slow fibrillation was recorded by the electrocardiography (Fig. 2). Inasmuch as 20 mg. of procaine had been given twelve and three minutes before the episode of cardiac arrest, it was thought possible that the arrest was due to an abnormal response to a small dose of the drug, therefore it was not administered again but rather Neo-synephrine approximately 1 c.c. within the chamber of the right ventricle, and approximately 0.5 c.c. into the wall of each ventricle, followed within fifteen seconds by ventricular dissociation, then by the resumption of relatively normal beats at 88 a minute, and blood pressure 50/40, after 4 gr. of intravenous aminophylline. The patient seemed to stabilize with a blood pressure of 80/60 with a ventricular rate of 125-200. It was decided to carry on with the planned procedure, since it seemed unlikely that the patient would survive unless mechanical improvement was afforded the heart. The punch valvulotome (Fig. 3) was inserted without recovery of tissue; in doing this the auricular appendage was torn and there was considerable blood loss. The reverse scissors type of valvulotome (Fig. 4) was next inserted and incision with the cutting blade carried through the medial commissure. Again there was marked blood loss through the open appendage. The total blood loss was approximately 1,500 c.c. Hemostasis was extremely difficult by digital compression but control was

obtained and a No. 3 silk tie was secured about the base of the appendage. The pericardium was loosely closed. The chest wall closure was completed in layers with interrupted 000 black silk sutures. At the time the skin was closed, the patient had a blood pressure of 80/60 and a pulse rate of 140. Three and one-half hours later, the pulse was 100 and the blood pressure 110/60. At this point, the electrocardiogram resembled those taken before the operation.

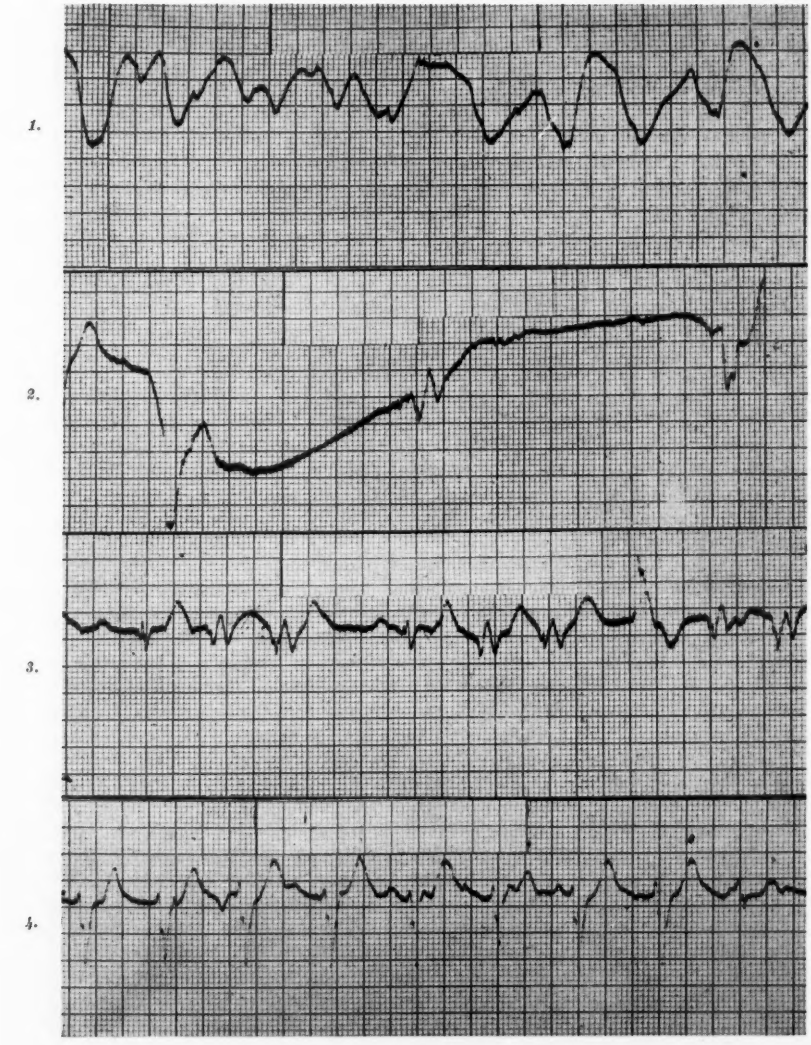

Fig. 2.—Electrocardiographic tracings during valvuloplasty No. 3. From above downward they show (*1*) bizarre ventricular activity due to slow ventricular fibrillation and the mechanical effect of cardiac massage; (*2*) very slow bizarre ventricular complexes; (*3*) idioventricular rhythm with several foci of impulse formation and possible auricular activity; (*4*) idioventricular rhythm or auriculoventricular nodal rhythm and intraventricular block with apparent auriculoventricular dissociation.

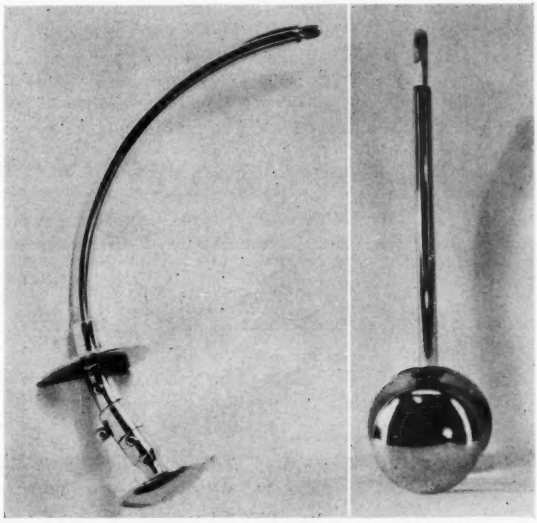

Fig. 3.—The cardiovalvulotome of the punch type.

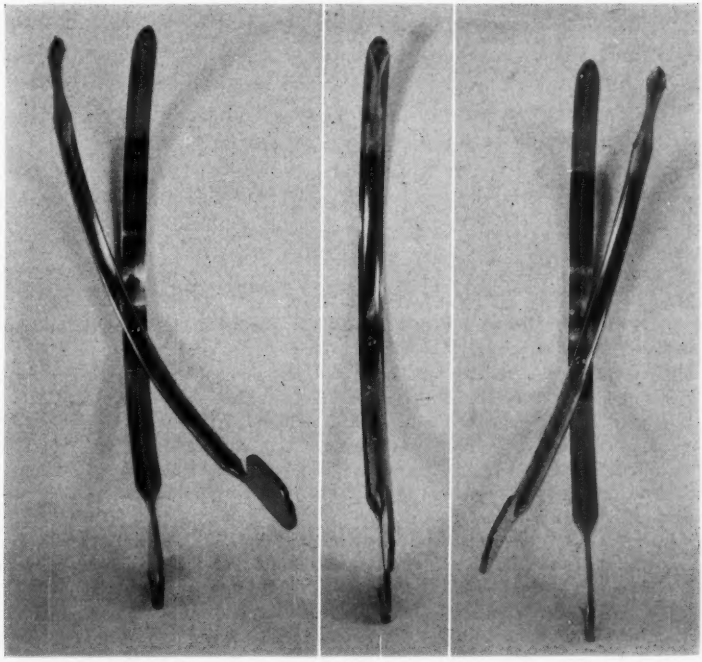

Fig. 4.—The reverse scissors type of valvulotome. The upper blade is the cutting blade. The lower guard blade affords opposing counterpressure for cutting in either direction.

The postoperative course was surprisingly uneventful. There was a marked change in the character of the apical cardiac murmur to a harsh systolic and a faint, short diastolic without presystolic accentuation.

The patient was able to be up and about the ward on the eighth day after operation and even then felt able to perform greater physical effort than before the operation. She was discharged from the hospital on February 12. Two months after operation, she was able to climb stairs for the first time in two years and to perform graded exercises with much less dyspnea.

Postoperative catheterization studies are shown in Table I.

TABLE I. F. M. (MITRAL STENOSIS CASE 6, VALVULOPLASTY NO. 3)

	CARDIAC INDEX	STROKE VOLUME (C.C. PER BEAT)	PULMONARY ARTERY PRESSURE (MM. HG) SYSTOLIC	DIASTOLIC	MEAN
Preoperative (12/28/48)					
Resting	2.43	50.0	77.5	30.5	49
After exercise	2.92	36.5	122.5	64.5	74
Postoperative (3/16/49)					
Resting	2.84	46.5	50.0	21.5	32
After exercise	3.18	49.0	73.8	31.5	46

Comment.—This record is significant for several reasons. Not only can an extremely ill patient survive mitral valvuloplasty, but there is unmistakable objective evidence of improvement following this operation. Survival alone is not a sufficient assay of surgical success.

There are perhaps only two previous examples of ventricular fibrillation on the operating table, proved by electrocardiography, that have reverted to effective beat coincident with maneuvers on the part of the surgeon directed at defibrillation of the heart (Beck[25] and Lampson[26]).

Finally, the lack of control of blood loss from the auricle after it was torn emphasized the grave need for more dependable means of grasping and fixing this structure as well as more deliberate hemostatic means of introducing instruments into the heart.

Mitral Stenosis Case 7, Valvuloplasty No. 4.—E. C., a 36-year-old white married woman, entered the Boston City Hospital Feb. 11, 1949. This was her ninth hospital admission with chief complaint of hemoptysis.

Thirteen years prior to this admission, she first noted bloodstreaked sputum, with increasing fatigability. Several months after the onset of symptoms, she had a massive hemoptysis, at which time she was told she had serious heart disease. There was no history of acute rheumatic fever. Digitalis was begun at that time, and has been continued since. Since the initial episode, she has had recurrent bloody sputum, difficulty in breathing, and has led the life of an invalid at home and in hospitals. Her hospital admissions were necessitated by episodes of pulmonary edema.

Since the last hospitalization one year before admission, she has suffered dyspnea on walking a few feet, marked orthopnea, frequent attacks of paroxysmal nocturnal dyspnea, and mild intermittent ankle edema.

On the night before this admission, the patient vomited several times, noted tachycardia with palpitation, and gradual increase in dyspnea accompanied by frothy pink sputum. She was admitted in acute pulmonary edema with evidence of a pulmonary infection. She responded to therapy, including oxygen, sedatives, antibiotics, and diuretics.

Physical examination when she was convalescent two weeks later was as follows: Her appearance was that of an emaciated 36-year-old woman. The general physical examination was not remarkable except for the cardiovascular examination. The lungs were clear. The heart was enlarged to the left, and there was no evidence of peripheral congestion. There was a diffuse precordial thrust with an apical presystolic thrill. Over the mitral area was heard a diastolic rumble with crescendo presystolic murmur and a loud mitral first sound. The second pulmonic sound was loud and split. The rhythm was regular, heart rate 98. Blood pressure was 100/54.

Teleroentgenograms and fluoroscopy revealed marked enlargement of the pulmonary artery at the conus, increased arterial markings in both lung fields, and enlargement in the transverse diameter. Electrocardiograms gave evidence of right ventricular enlargement. The hematocrit was 40, the hemoglobin 14 Gm. The white blood cell count was 7,350.

Cardiac catheterization showed the cardiac output to be 4.57 liters per minute (cardiac index, 3.06) with no appreciable change in output or stroke volume on exercise. Pulmonary artery pressures were not obtained.

Mitral valvuloplasty was done March 14, 1949. Premedication was Seconal 0.40 Gm., demerol 100 mg., scopolamine 0.65 mg. Anesthesia was cyclopropane induction, then endotracheal ether.

Electrocardiographic tracings were followed throughout.

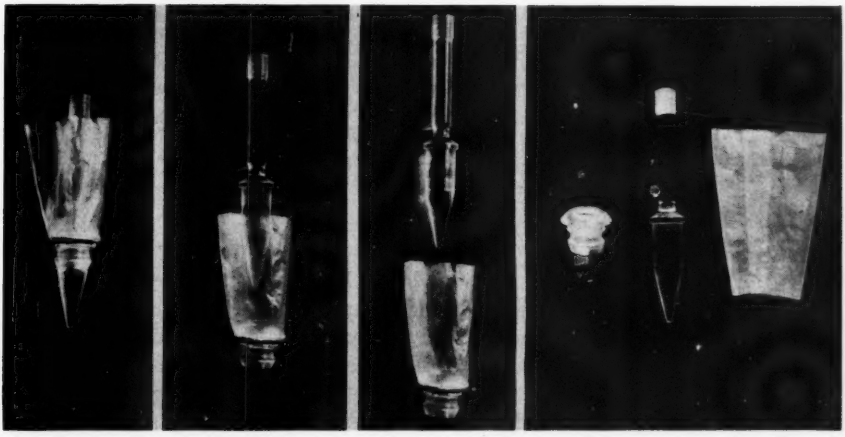

Fig. 5.—The operating tunnel with introducing obturator and plastic control sleeve.

With the patient in the dorsal decubitus position, a curved 34 cm. incision was carried from the left sternal border below the left breast to the anterior axillary line. The breast was reflected upward and the chest opened in the third intercostal space. The costal cartilages of the third and fourth ribs were divided 1.5 cm. to the left of the sternum and the ribs spread. The pericardium was opened anterior to the phrenic nerve and silk marsupializing traction sutures were placed. A greatly enlarged pulmonary artery measuring perhaps 6 cm. in diameter presented and caused cardiac rotation that gave the left auricular appendage a posterior position. This position of the appendage necessitated a second incision posterior to and parallel to the phrenic nerve, and thus afforded adequate appendage exposure. The margins of the auricular appendage were grasped by two Kelly clamps, the auricle between the clamps was incised, and the operating tunnel inserted (Fig. 5). A silk suture of No. 2 silk previously laid at the base of the appendage was then tied, but was not properly placed and the polythene cuff of the tunnel occluded. Efforts at using the well were abandoned. There had been little blood loss and the patient's condition remained good.

The curved valvulotome punch was then directly introduced with considerable blood loss (perhaps 1000 c.c.). Two bites of the mitral valve were taken. The blood pressure fell rapidly, but the heartbeat remained regular. Pressure transfusion brought the blood pressure to normal levels within ten minutes. It was felt that the valvular excision had not been adequate so the valvulotome was reintroduced and another bite taken. This was again accompanied by marked blood loss, at least 1,500 c.c., and the patient went into shock.

Although there was marked bleeding during the intracardiac manipulation, it was twice demonstrated that the auricle clamp (Fig. 6) worked nicely in controlling blood loss between manipulations. During and following these manipulations 3000 c.c. of blood were delivered under pressure, but we did not feel that the rapid replacement technique was as satisfactory as it might have been.

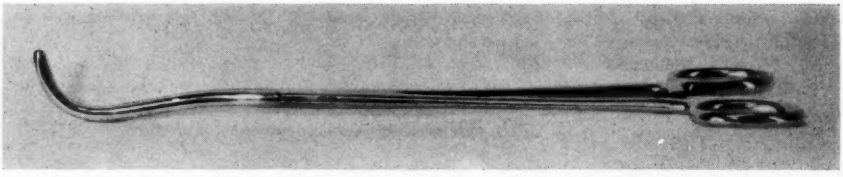

Fig. 6.—The auricle clamp—a noncrushing clamp with teeth to prevent slipping.

With the onset of shock, the heartbeat became irregular, there was auriculoventricular block recorded by continuous electrocardiogram, then idioventricular rhythm, and finally ventricular arrest and fibrillation. Cardiac massage was instituted, positive pressure respiration conducted, Neo-synephrine injected intracardially, and finally, electric shock applied. All measures were futile. Massage and artificial respiration were continued for thirty minutes without resumption of autogenous activity. Permission for post-mortem examination was not obtained.

Comment.—This case illustrates the devastating effects of hurried, blind operating with inadequate control of blood loss. The auricular incision and therefore subsequent blood loss was much larger than in any other operation because the well had been inserted and removed. Doubtless the operating well should not have been abandoned after one simple initial complication in insertion. Certainly in retrospect we can say that the second intracardiac maneuver should not have been attemped.

Mitral Stenosis Case 8, Valvuloplasty No. 5.—M. H., a 29-year-old male veteran, was admitted to the Peter Bent Brigham Hospital on Feb. 21, 1949, for evaluation of his cardiac status.

Seven years previously, in November, 1942, he was refused admission to Officer-Candidate School because of a "presystolic murmur." Army discharge followed shortly. The patient had few complaints until years later. In 1945, he began to suffer from pains over the precordium associated with dyspnea that was frequently asthmatic in character. These increased in severity over the next two years. Late in 1946, hemoptysis occurred and varied from streaking to frank hemorrhage of 750 c.c. At this time the patient was admitted to a Veterans Administration Hospital, where he was observed for nine months. During the course of this hospitalization there were occasional episodes of bleeding. At times he had a low-grade fever and lesions suspected of being petechial in character were noted. The patient was digitalized at this time and has continued on 0.2 mg. of digitoxin daily since. He was given ammonium chloride, Mercuhydrin, and salicylates. Following his discharge from that hospital in September, 1947, he was fairly comfortable for a few weeks until pain, dyspnea,

and hemoptysis reappeared. The patient said that he had thirty episodes of hemoptysis from the end of 1947 until his hospital admission to the Peter Bent Brigham Hospital. He had a weight loss of forty-eight pounds in five years. Weight at time of admission was 106 pounds.

Past history revealed scarlet fever and pneumonia in 1927. There were four other attacks of "pneumonia" during the next ten years and following that, in 1937, there was a migratory arthritis characterized by pain and swelling with no redness or heat, involving knees, elbows, shoulders, and hands.

Physical examination revealed a well-developed, poorly-nourished, agitated, and apprehensive man. Lungs were clear to percussion and auscultation. The neck veins were distended, and there was pulsation of the arteries of the neck. A marked apical thrust was noted over the point of maximum impulse in the sixth intercostal space at the anterior axillary line, 13 cm. to the left of the midsternal line. The rate was 100, rhythm normal. There was a rumbling diastolic murmur with a presystolic accentuation over the mitral area; the mitral first sound was loud and snapping. A Grade II systolic murmur, heard in the third intercostal space, just to the left of the sternum, was believed pulmonic in origin. In addition there was an aortic systolic murmur. The second aortic and pulmonic sounds were reduplicated. The liver margin was four fingerbreadths below the costal margin in the mid-clavicular line. "Liver palms" and fingers were noted. Blood pressure was 105/65, temperature 98.6.

Teleroentgenograms revealed a heart enlarged to the left and right, with an estimated 20 per cent increase in transverse diameter. The left auricle was markedly enlarged posteriorly. The contour was consistent with rheumatic heart disease and mitral stenosis. Laboratory studies indicated a red blood cell count of 4,090,000, and hematocrit of 50. The white blood count was normal. Sedimentation rates ranged from 5 to 50. The higher levels were thought to be associated with cystitis, hemoptysis, and pulmonary edema. The vital capacity was 3,500 c.c. The venous pressure was recorded as 150 mm. of saline solution. Circulation time, Decholin (arm to tongue) was 17 seconds; ether (arm to lung) was 7 seconds. Electrocardiograms revealed the auricular complex to be abnormal with incomplete right bundle branch block.

Cardiac catheterization revealed a cardiac output at rest of 4.6 liters (cardiac index 3). The stroke volume was 43 c.c. The mean pulmonary capillary pressure rose from 18 mm. Hg to 32 when the heart rate rose from 100 to 120. Pulmonary artery pressure was 40 mm. systolic, 18 diastolic. Exercise studies were not carried out because of the marked debility of the patient. Further detailed laboratory study revealed a normal electrolyte pattern.

During the course of investigation, the patient had episodes of pulmonary edema and hemoptysis. Dibenamine did not slow the pulse rate. In the light of the rapid deterioration of the patient with no response to medical treatment, and studies pointing to obstruction of the mitral valve as the dominant lesion, the direct operation was advised.

Mitral valvuloplasty was done March 18, 1949. Premedication was Nembutal 0.1 Gm., morphia, 0.01 Gm. Quinidine, 0.3 Gm., was given two hours before surgery. Anesthesia was brief pentothal induction, then endotracheal ether.

Electrocardiographic tracings were followed throughout the procedure. Cannulae were tied in veins at both ankles to afford opportunity for rapid transfusion.

With the patient in semi-Fowler's position, the left side of the chest elevated, a 30 cm. incision was carried over the third intercostal space from the sternum to the anterior axillary line. Pectoral muscles were split and the third and fourth costal cartilages were divided after entering the left thoracic cavity through the third interspace. During the spreading of the ribs 20 mg. of procaine in a 1 per cent solution were given intravenously to reduce the frequency of ventricular premature beats.

The pericardium was opened 1 cm. above and parallel to the phrenic nerve. This afforded good exposure of the left auricular appendage. The pulmonary artery was enlarged, having a diameter of approximately 5 cm. The tip of the appendage was grasped with two Kelly clamps after fibrous adhesions between the appendage and the pulmonary artery had been freed manually. The auricular appendage was incised between the clamps and through

this incision the operating tunnel was inserted. The auricular wall was tied in place with a No. 5 black silk suture. Little blood was lost during this maneuver.

The curved punch valvulotome was introduced through the operating tunnel, the mitral fishmouth located, and two substantial cuts were made in a region taken to be that of the posterior leaflet. Segments of valve leaflet on the zones of fused commissures were not removed in the valvulotome. The valvulotome was introduced twice. The second time the punch was inserted tiny fragments of tissue resembling bits of chordae tendineae were found in the instrument. A No. 5 black silk tie was then placed about the base of the appendage and the suprajacent portion was cut off to recover the tunnel. At this point, the blood pressure had fallen beyond detection and the heart action became so feeble as to suggest impending arrest. However, after a rest period of five minutes the action had recovered sufficiently that a blood pressure of 80/40 was obtained and the continuous electrocardiogram showed a regular rate of 104 beats a minute.

The pressure in the auricle was not taken because the trocar used for such soundings had perforated the plastic sleeve of the tunnel and also had damaged the wall of the left auricle. Both of these perforations resulted in blood loss that made the intracardiac maneuvers less than completely deliberate. Blood loss through the laceration of the auricle was controlled by pressure with an Oxycel sponge and the sleeve perforation was occluded by digital compression until the auricular appendage had been tied and amputated.

The pericardium was then loosely closed, leaving the Oxycel sponge on the auricle at the point of perforation.

Approximately 1,200 c.c. of blood were aspirated from the left pleural space, the lung was expanded, and 400,000 units of penicillin were instilled. The chest wall was closed with interrupted silk sutures, without drainage.

The left auricular appendage removed at operation showed histologic changes consistent with an active rheumatic carditis. These included perivascular foci of oval vesicular cells believed to represent Aschoff bodies.

The postoperative course was moderately stormy, due primarily to the patient's limited respiratory reserve, to great apprehension attending discomfort, and to considerable bloody effusion in the left pleural space.

After four days of apparent improvement, he suddenly went into pulmonary edema and died within a few hours in spite of standard therapy.

Gross autopsy findings were essentially those of far-advanced stenosis with the pulmonary vascular changes that may be associated with this condition. The valvulotome had produced a defect 3 by 1 mm. in the medial commissure and a much smaller defect, virtually a scratch of the lateral commissure. The classical marginal ring at the vortex of the funnel that prevents mitral valve opening or closure had not been broken. The stenosis had not been corrected by valvuloplasty, nor had it been significantly altered by "selective insufficiency."

Comment.—The operative and autopsy findings in this patient re-emphasize some cardinal features of the pathology and surgical technique in the correction of mitral stenosis.

The operating well was used successfully here; it may make intracardiac maneuvers more deliberate, with better control of blood loss. We look forward to using the operating tunnel as the portal through which damaged valves may be excised and prosthetic valves be inserted. Hufnagel is now making significant progress in the use of plastic valves.[27]

In this operation, alarming evidence of ventricular irritability and disturbances of electrical conduction developed when the ventricular endocardium was stimulated. This has become apparent by correlating our direct observations of the heart at operation with the continuous electrocardiogram, and by repeated observations during cardiac catheterization.

The microscopic finding of active rheumatic carditis points out the need for clinical tests for assessing disease activity. By our own criteria, we should not have selected this patient for surgery had we been able to predetermine the presence of such activity.

At autopsy, it was revealed that the mitral valve did not have a diffuse calcific thickening of the fishmouth funnel. Most of the patients with mitral stenosis that we have seen at autopsy have not had such calcification. They have had thickened leaflets, to be sure, but large areas of the leaflets have been thin to the point of translucency and quite flexible. This cannot be readily appreciated in specimens after fixation in preservative. The significant point in stenosis is rather the marked thickening in a *ring* of dense fibrous tissue at and just back of the free margin. This fibrous ring is continuous across the fused commissural zones. At the point of the fused commissures *this ring prevents the closure of the valve in systole,* just as it prevents opening of the valve in diastole.

It appears to us that we can expect considerable improvement in the valvular action of the thickened mitral funnel if this ring is broken, preferably by incision or wedge resection in both commissural zones (Fig. 1). This allows some restoration of function to the thickened leaflets. Obviously, the thickening and shortening of the chordae tendineae, the papillary muscles, and the leaflets themselves may preclude the restoration of perfect valvular function.

This concept of the nature of the mechanical difficulty in mitral stenosis throws considerable light on the reason for the high mortality in the surgery of the disease. If this sort of major surgery is performed without correction of the mechanical handicap, a *properly selected* patient is in no condition to withstand the operation. Conversely, it would appear that patients can withstand valvuloplasty if it does properly improve the underlying valvular disease. The second and third patients in the valvuloplasty series, who were the gravest of risks and operated upon during a period of pulmonary edema, demonstrated this fact.

DISCUSSION

Our experience with mitral stenosis now involves a study group of twenty-five patients, eight of whom have been treated surgically. There have been three surgical deaths. The operations have been as follows: Five valvuloplasties, two interatrial septal defects, and one denervaiton. The deaths were all in the valvuloplasty group. The first patient of the series was lost because we did not at that time appreciate the devastating effect of tachycardia. The second death was the fourth valvuloplasty. This death was on the operating table from uncontrolled blood loss. The third death was from pulmonary edema on the fifth postoperative day, and autopsy revealed that too little valvuloplastic incision had been made. This debilitated patient was therefore subjected to a very strenuous operation without the relief of adequate correction of the fundamental mechanical handicap.

The experience to date seems to indicate that essential knowledge of the technical difficulties and the indications for various surgical procedures is being gathered.

The possibility of practical surgical relief of mitral stenosis calls for more complete understanding of the disease. Means must be sought to predict the probable clinical course of a given patient. Those who have a truly malignant form of valvular disease should be selected, if possible, before the pulmonary changes render the patient an inordinately serious risk for surgical intervention.

Objective evaluation before, during, and after operation must be conducted in order to determine which procedures are best tolerated and most beneficial. These appraisals should include detailed observations of the cardiac and pulmonary dynamics, both at rest and during exercise.

SUMMARY

1. A tentative classification of patients suffering from mitral stenosis and the operations considered appropriate in those conditions is discussed.

2. Three additional patients who have had valvuloplastic operations have been presented.

3. One of the new patients has completed postoperative evaluation and shows conclusive improvement associated with the valvuloplastic operation.

4. The total experience with 25 patients in the study group has been mentioned in relation to 8 patients who have had surgical treatment. The 8 patients have had the following operations: 5 valvuloplastic procedures, 2 shunts through the provision of septal defects, and 1 cardiac denervation. There were 3 surgical deaths, all following valvuloplasty.

5. An operating tunnel is presented. This tunnel provided an opportunity for more deliberate, better-controlled intracardiac operation in a human valvuloplasty.

6. The mechanical problem posed by the thick marginal ring of fibrous tissue seen in mitral stenosis is reviewed.

7. Two additional principles of mitral valvuloplastic surgery have been presented:

V. Blind intracardiac maneuvers must be well controlled and deliberate.

VI. There must be least possible stimulation of the ventricular endocardium during intracardiac operation.

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(See page 45 for discussion)

THE SURGERY OF MITRAL STENOSIS

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IT WAS inevitable that the many recent advances in cardiac diagnosis and surgery would shortly foster invasion of the heart chambers. Whereas cardiac surgery for the most part has been the surgery of the great vessels encompassing the heart and as such might better have been termed cardiovascular surgery, recent intracardiac invasion has re-affirmed its right as a definitive entity. The eventual scope of such endeavor is limited only by the anatomical boundaries of the organ itself, and by the enlightened intrepitude of its invaders.

It is logical that chronic valvular disease of the heart should be among the first intracardiac disorders subjected to surgical attack. It is common and found universally. White[1] has estimated that 0.5 to 1 per cent of the community is affected, particularly in those areas where rheumatic fever is endemic such as in the northeastern part of the United States and Northern Europe. The great majority of persons who have had rheumatic fever (about 85 per cent) develop deforming valvular disease of the heart, the mitral valve being most frequently affected. Organic stenosis of the mitral valve is probably the commonest single end result of rheumatic infection, although organic aortic valve disease in the form of a regurgitant lesion is rated an equal by some.

The prognosis of an individual case of mitral stenosis depends upon many factors: the age of the patient, the severity of the lesion, the presence or absence of other valve defects, the presence or absence of additional rheumatic activity, and the condition of the myocardium. The ultimate outcome, however, is almost invariably unfavorable. Not only is the life span shortened, but handicapped activity, invalidism, and occasionally vegetation are present among its victims. Although a few may escape until later years, it is more often fatal before or soon after the patient reaches adult life. Recently we have been consulted by a 58-year-old woman who had been apparently "successfully" treated over a period of thirty years. Indeed, she had been skillfully managed, for which she was grateful; yet she plaintively requested surgery at this late date, for while she had lived, "It wasn't like a life. I never could do anything."

Since medical therapy has so little to offer in many cases, and since a stenotic lesion is essentially a mechanical stricture, it is little wonder that direct surgical attack was suggested by Brunton as early as 1902.[2] The ideal approach to such a problem can be directed only at correction of the stenotic valve itself, provided this can be accomplished without the production of deleterious side effects. Should such attempts fail, satisfactory relief might be forthcoming by less definitive but fairly adequate indirect methods. When a condition is recognized as offering only a fatal or hopeless outlook, desperate measures seem less desperate and with application and courage not infrequently can be made safe.

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ANATOMIC, PATHOLOGIC, AND PHYSIOLOGIC CONSIDERATIONS

The interplay of these three factors with reference to the mitral valve may seem complicated, but when reduced to essential components is readily understandable. One may think of the normal mitral valve as a truncated cone or megaphone composed of thin, flexible membrane. Its apical portion is suspended by many guy wires (chordae tendineae) which are grouped more heavily in two areas—one on each side of the apex of the cone. These areas represent the anatomic fusion of the two components of the valve (an anteromedial and a posterolateral leaf), and when modified by rheumatic disease become the "commissures." The entire cone is somewhat flattened toward the apex and these "commissures" represent the lines of folding (lateral seams of the megaphone) of the valve structure. The plane of flattening is neither horizontal nor vertical as the patient lies supine, but is rather sharply oblique. The anteromedial cusp is larger than the posterolateral, lies diagonally anterior to it, and is continuous with the posterior wall of the intracardiac portion of the aorta. In auricular systole the posterolateral cusp lies well away from the lateral ventricular wall, but during ventricular systole may approximate it. For this reason, mitral regurgitation is primarily a dysfunction or defect of the anteromedial cusp of the valve. Contraction of the papillary muscles synchronous with ventricular contraction draws the chordae tendineae taut and prevents the valve leaflets from becoming inverted or displaced backward into the auricle.

In rheumatic disease the mitral valve develops numerous minute cauliflower-like vegetations (1 to 2 mm. diameter) in a row along the line of closure of the valve. Healing leads to the formation of scar tissue. With repeated infection and healing there is gradual development of fibrosis, thickening, narrowing, and shortening of the apical one- to three-quarters of the mitral cone. The apical end becomes fixed in the infolded or flattened position, so that the "commissures" become an anatomic reality. Since the fibrosis and fixation of the orifice take place during constant heart motion, the orifice assumes a slightly oval shape. Thus, in a well-developed stenotic lesion the valve is reduced to a rigid slit in a fibrotic plaque. There is then marked resistance to the passage of blood from the left auricle into the left ventricle. There is also, inevitably, some degree of regurgitation of blood into the left auricle through the rigid slit during ventricular systole.

When this regurgitation is minimal, such a lesion is considered to be one of "pure" mitral stenosis. Such a "pure" lesion markedly interferes with left ventricular filling and thus with systemic cardiac output. Many such hearts are unable to increase their output over and above the resting bodily requirements. It is easy to understand why such hearts cannot perform any appreciable amount of work, and why patients with such hearts become dizzy and faint upon exertion.

Concurrently, since the egress of blood from the left auricle is impaired, increased pressure within and great dilatation of this chamber results. The high intra-auricular pressure is transmitted to the entire pulmonary vascular system and thence to the right ventricle. A chronic pulmonary hypertension ensues, with eventual rupture of pulmonary capillaries (hemoptysis), pulmonary edema (dyspnea), and right heart failure (enlarged liver, ascites, and peripheral edema).

SURGICAL CONSIDERATIONS

The possible surgical approaches to the problem of mitral stenosis seem to take one of the following three courses:

1. Methods of by-passing the stenotic mitral valve
2. Methods of relieving the associated pulmonary hypertension
3. Methods of direct surgical attack upon the stenotic valve

Methods of By-passing the Stenotic Mitral Valve.—To our knowledge very little has been attempted or accomplished along the lines of by-passing the mitral valve. Jeger[3] suggested in 1913 that a valved vein might be grafted to serve as an anastomosis between the pulmonary vein and the left ventricle, and thereby adequately sidetrack the stenotic mitral valve. Litwak,[4] working in our laboratory, has been able to produce such a by-pass by anastomosing a pulmonary vein directly to the left ventricle, utilizing a free graft of azygos, hemiazygos, or femoral vein. This was accomplished in five dogs with function observed for several days, but all became thrombosed within two weeks to one month (Fig. 1).

Fig. 1.—Azygos vein graft from inferior pulmonary vein (below) to the lateral wall of the left ventricle (above) produced in the experimental animal.

Satinsky,[5] also in our laboratory, attempted quite a different type of by-pass. He divided the subclavian artery in dogs and anastomosed the distal end of this vessel to a pulmonary vein. Similar anastomoses of the pulmonary vein to the splenic artery and aorta were also attempted. These operations were deleterious to normal dogs, causing death, but conceivably might be of some value were the conditions of clinical mitral stenosis present.

Methods of Relieving the Associated Pulmonary Hypertension.—Various methods have been devised to relieve the associated pulmonary hypertension which accompanies mitral stenosis:

(1) Harken[6] has suggested that a measure of improvement may be afforded by removal of the cardiac accelerator and afferent nerves to the heart. Relief so obtained is through the production of a slower heart rate, thereby increasing ventricular filling time, or by the interruption of pain fibers. He has observed symptomatic relief in a patient so treated, but suggests that such an approach can obviously only be one of palliation. We have had no experience with this form of treatment.

(2) Attempts have been made to destroy the function of the tricuspid valve with the production of tricuspid regurgitation to prevent easy access of blood into the right ventricle and lower its pulmonary output.[7] In our opinion such an approach has little to recommend it.

(3) The production of a communicating shunt between the pulmonary and systemic venous systems, thus affording a measure of relief to the hypertension within the left auricle, has some merit. An anastomosis between the azygos and pulmonary veins has been accomplished by Sweet[8] with subjective relief of distressing pulmonary symptoms.

(4) Both Harken[9] and our group have produced interauricular septal defects to relieve the pulmonary hypertension of mitral stenosis. Such a venous shunt will reduce the hypertension and strain within the left auricle and, secondarily, the associated hypertension throughout the pulmonary vascular bed. Bing[10] and our laboratory have obtained pressure readings within the pulmonary artery in certain cases of mitral stenosis which were higher than that within the aorta (120+ mm. Hg). Theoretically, a venous shunt should relieve strain on the entire lesser circulation, and one would anticipate relief of such symptoms as hemoptysis and acute attacks of pulmonary edema. It is probable that such an effect is accomplished to a degree.

Unfortunately, reduction of the left intra-auricular pressure without enlargement of the mitral orifice results in a destruction of the compensatory mechanism which nature has set up to force blood through the narrowed mitral valve. With the production of such a shunt, the left ventricular output falls. The amount of fall is related to the relative sizes of the shunt orifice and the mitral orifice. Obviously, no case can withstand a shunt if the cardiac output during exercise does not materially increase over the resting requirements. By the same token, it is essential even in those who can so increase their output, that this should not be cut below the level of resting requirements. Since most clinical cases can do no more than double their resting output, it follows that one should not produce an opening even as large as the stenotic mitral orifice unless it is planned to render the patient totally bedfast.

It has been repeatedly stated that Nature, herself, has produced a similar combination of defects in the form of Lutembacher's syndrome. Indeed, the syndrome does embrace both a mitral stenosis and a large auricular septal defect. In this instance it must be remembered that compensation has been established

over many years by gradual changes in the heart and by a great increase in the total blood volume. These patients are said to do well, or at least somewhat better than do cases of "pure" mitral stenosis. Taussig,[11] with reference to this syndrome, stated that, "The blood so shunted [through the auricular septal defect] passes into the right ventricle and thence is pumped out through the pulmonary artery to the lungs and is again returned by the pulmonary veins to the left auricle. Thus an excessive amount of blood is pumped around and around the lesser circulation; whereas the left ventricle, aorta, and systemic circulation receive less than their normal quota of blood. The right auricle and ventricle are enlarged. The pulmonary artery is usually twice the size of the aorta. The strain on the left auricle is relieved by the defect in the auricular septum. Therefore, the left auricle is not enlarged. The left ventricle is small." Thus, for a time the strain on the left auricle and pulmonary vascular bed may be somewhat relieved, but only at the expense of producing a similar strain on the right ventricle, a condition equally serious. Again quoting Taussig,[11] "The

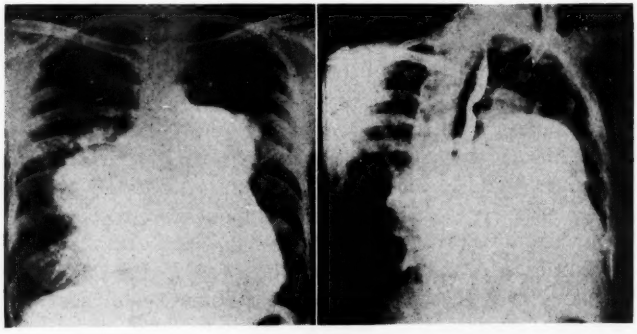

Fig. 2.—Lutembacher syndrome showing enormous dilatation of the pulmonary artery. Anteroposterior and right anterior-oblique positions. (From Taussig: Congenital Malformations of the Heart, Commonwealth Fund.)

late development of cardiac difficulties [in Lutembacher's syndrome] occasionally occurs after a relatively minor illness. For example, a patient who has never been known to have any cardiac abnormality, after some *slight* illness may suddenly develop symptoms which lead to progressive heart failure." (See Figs. 2 and 3.) It would seem that any condition which caused such great pulmonary arterial and right ventricular enlargement can scarcely be considered desirable. Actually this defect terminates fatally at the average age of 40 years —slight, if any, improvement over longevity in uncomplicated mitral stenosis.

Indeed, the production of a venous shunt for mitral stenosis seems somewhat comparable to the production of an arterial shunt (systemic artery to pulmonary artery) for the treatment of congenital pulmonary stenosis. The production of an artificial ductus arteriosus is lifesaving in cases of severe pulmonary stenosis. However, too large a shunt is promptly fatal, and any arterial shunt increases the load on the myocardium, leading to eventual cardiac enlargement. Helpful as these shunts have been, if a method of direct and successful attack upon the

pulmonary stenosis were to become available, we have no doubt that all concerned would promptly embrace the more direct procedure. It would then be necessary, although perhaps not practicable, to recall these cases for the performance of direct valvular surgery and subsequent division of the artificially produced "patent ductus arteriosus." So, too, with the venous shunt. If such shunts are created to save life in the face of demonstrably superior direct valvular attack, we will soon be faced with the problem of repairing these shunts.

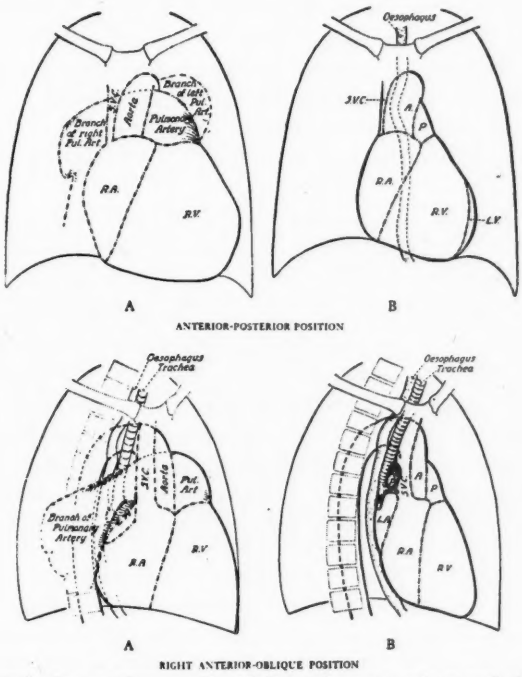

Fig. 3.—(*A*) Lutembacher syndrome with dilated pulmonary artery and (*B*) normal heart, adult. (From Taussig: Congenital Malformations of the Heart, Commonwealth Fund.)

Methods of Direct Surgical Attack Upon the Stenotic Valve.—Direct attack upon the mitral valve undoubtedly has been contemplated for many decades. It was proposed by Sir Lauder Brunton[2] in 1902. Being a physician and not a surgeon, he had to be content with suggesting that the only proper and logical approach to the problem of mitral stenosis was to "lengthen the slit." How sound his judgment was will become evident shortly.

Since the first section of the mitral ring by Cutler[12] in 1923, there have been a number of direct attacks upon the stenotic mitral valve. The approach and the methods employed have varied. Thus, the left auricular appendage as a site of entrance has been utilized by Allen and Graham, 1922[13]; Souttar, 1925[14]; the authors, 1945; Smithy, 1948[15]; and Harken, 1948[6]; the left ventricle by Cutler, Levine, and Beck, 1924[16]; Pribram, 1926[17]; Smithy, 1948[15]; and through the left

pulmonary vein by Harken, 1948.[6] It is our considered opinion that the approach through the auricular appendage is far superior to any other. It leads directly into the wide opening of the mitral funnel and thence to its stenotic orifice. There are no chordae tendineae to interfere with the passage of the instrument or finger. In addition, no serious disturbance of cardiac rhythm or function is produced. The finger or instrument is well tolerated in the roomy left auricle, unless the actual passage of blood into the ventricle is obstructed for more than three beats. In addition, the appendage may be readily and securely ligated at completion of the operation.

On the other hand, the left ventricular approach is obstructed by chordae tendineae and does not insure ready or accurate localization of the small opening of the mitral funnel. Such an approach may provoke a serious arrhythmia, does not permit digital insertion or palpation, and may be difficult to close securely.

Approach through a pulmonary vein is less desirable than the auricular route, but may be an improvement over the ventricular method provided the vein is not so damaged as to require ligation.

Methods of dealing surgically with the valve have included (1) simple incision of a valve cusp, (2) excision of a portion of the mitral ring, (3) digital dilatation of the stenotic orifice, (4) valvuloplasty, and (5) commissurotomy.

Simple incision of a mitral valve cusp has a very deleterious effect upon the experimental animal. If the anteromedial or "aortic" cusp of the mitral valve is completely divided, death is prompt and almost immediate. If the posterior cusp is completely divided, death is usual within twenty-four hours. While Cutler's first patient lived four and one-half years after simple incision, it appears that he did not completely divide the cusp. Dogs, too, will tolerate lesser degrees of valve section. One of the objections to simple incision of the ring is the possibility of healing at the site of the incision. It seems improbable that such healing would occur if the valve ring were widely incised, since the edges would then gape widely during most of the cardiac cycle. On the other hand, if the incision extended only partially through the scar tissue, it could not gape and very probably healing and further cicatrix would occur. Of three such cases reported by Cutler, Levine, and Beck,[16] two died shortly after surgery. Contained in this report are two additional cases, both of whom died from severe regurgitation (Cases 8 and 9).

Simple excision of the valve ring was practiced by Cutler and Levine, 1923[18]; and Cutler, Levine, and Beck[16]; also by Pribram, and later by Smithy. Since it was felt that the only hope in mitral stenosis was to replace it by a regurgitant type of lesion, partial excision of the valve orifice seemed to be a logical procedure. We are unequivocally opposed to this concept, since experimentally and clinically it has been demonstrated that a suddenly produced mitral regurgitation is poorly tolerated and is as serious a lesion as the original stenosis. Bitter experience in two of the cases presented makes us adamant on this point (Cases 8 and 9).

Results by this form of treatment have been discouraging in the past. Thus, four patients so treated by Cutler, Levine, and Beck[16] and one by Pribram, all died within six days after operation. Smithy reported five living patients out of seven such operations in June, 1948. His better results may be attributed partially to advances in anesthesia and surgery since the work of the 1920's. More pertinent, however, is the fact that by design he excised relatively small pieces of valve tissue. Time will supply the answer as to how well his patients will carry on with their admitted regurgitation.

Digital dilatation of the stenotic valve was first practiced by Souttar in 1925 with success in one case. We have since performed three such dilatations with one success. The first of these was performed on June 12, 1946. A very hard, calcified valve slit in a practically moribund woman was dilated with marked temporary improvement. Death within three days was disclosed at autopsy to be due to clotting at the torn commissures. It was evident that the valve had torn at the line of the commissures sufficiently to establish some temporary valve function. Thrombosis had quickly re-established or increased the stenosis, causing death. At post-mortem examination the idea of cutting the commissures well into normal valvular tissue under direct digital guidance or "vision" was born (Case 2). Since that time we have had to resort to simple digital dilatation in two additional cases, with one success (Cases 12 and 13). We are well aware from studies upon stenotic mitral valves incidentally found at autopsy that simple digital dilatation does not always result in tearing the fused fibrotic commissures. The ring tears at its weakest point, which may well be across a cusp. Even when the tearing does occur at the commissures, one finger is seldom large enough to force the tearing to extend beyond the fibrotic tissue into normal valve structure. However, this early case of dilatation did result in what we then considered to be an entirely new concept of treatment. We now believe that Sir Lauder Brunton had much the same idea.

Harken[19] used the term *valvuloplasty* to describe his procedure of resection of portions of the valve ring at the commissures. He is still of the opinion that relief of stenosis is by the production of regurgitation. He rightly recognized that resection will best be tolerated if performed at the commissures, assuming that resection with regurgitation is the desired result. Two such operations have been performed. In one the pressure in the left auricle was 450 mm. water, but rose above the readings of a 500 mm. manometer after valvuloplasty of this type. This was attributed to a coincident tachycardia. The patient died in pulmonary edema twenty-four hours later. In the other patient, left auricular pressure dropped from 450 mm. water to 400 mm. during the procedure. He was improved subjectively. Localization of the commissures was accomplished by palpating the valve with the valvulotome inserted through the auricular appendage.

Commissurotomy is a term suggested to us by Dr. Thomas Durant of Philadelphia to designate the procedure which we have employed to re-establish a marked degree of normal mitral valve function.[24] Our present operative technique is simplified and direct. With the patient in the supine position, the left arm over the head, an incision is made over the left third rib or in the infra-

mammary fold. The third rib is removed, including the costal cartilage. The cartilages of ribs 2 and 4 may be divided. The pleura is opened through the incised rib bed. The lung is permitted to collapse. The pericardium is incised longitudinally, one-half inch anterior to the phrenic nerve, for three inches. Care must be taken not to extend the incision too far toward the apex, lest the heart have a tendency to herniate from its sac. The huge distended auricular appendage then protrudes (Fig. 4). After spraying 2 per cent procaine into the pericardial sac, it is injected under the epicardium, encircling the base of the auricular appendage (at the suggestion of Smithy). A purse-string suture of heavy braided silk on an atraumatic needle is passed about the appendage through this injected area. A Satinsky clamp[20] is then closed over the base of the appendage and a generous portion of its tip is amputated (Fig. 5). This piece serves for heart muscle biopsy. All intra-appendageal trabeculae that might interfere with insertion of the finger are divided. Two gloves are worn on the right hand. An opening is made in the outer one on the palmar surface at the base of the index finger, and another at the tip. The blade of the commissurotomy knife is inserted between the gloves (Fig. 6), on the index finger, and the finger is inserted into the left auricle as the clamp is released (Fig. 7). The finger is well tolerated by the auricle and causes no disturbance unless the mitral opening is actually obstructed by the finger tip for several beats. The valve is easily located, and is explored. Its structure is estimated, and the size of the opening and the location of the commissures are determined. The knife is then protruded through the orifice and the hook is engaged upon the anterolateral commissure (Figs. 8 and 9). A backward stroke divides the commissure, usually adequately the first time. The finger again palpates the opening and gently dilates it. Sometimes there are remaining fibrous strands which require either digital separation or actual division with the knife. If the cut in the commissure does not extend well into normal tissue it is repeated. In cases which have a rather soft valve orifice markedly diminished in cross-sectional area, simple opening of the lateral commissure is, in our opinion, sufficient. On the other hand, with a rigid, fixed, and sometimes calcified valve, incision of only one commissure would undoubtedly be inadequate.

We are indebted to Harken for a practical point brought to our attention recently with regard to the execution of our next maneuver. Prior to this suggestion, we had been using a metal sheath on the finger to permit changing from a left cutting to a right cutting knife and thus facilitate the division of both commissures. It was necessary by this former method markedly to supinate the wrist to incise properly the posteromedial commissure, and even then we had failed to cut this commissure properly in two cases. As a result, both of these patients died of severe regurgitation because the incision had been carried across the cusp slightly anterior to the medial commissure and into the so-called "aortic baffle"—the wall of the intraventricular portion of the aorta. One of these patients died within twenty-four hours, the other within three months. Autopsy disclosed the condition in both patients. There was no sign of healing of the incision in the longer surviving patient. Harken pointed out that by simply pronating the wrist the left cutting knife could be used for both commissures and

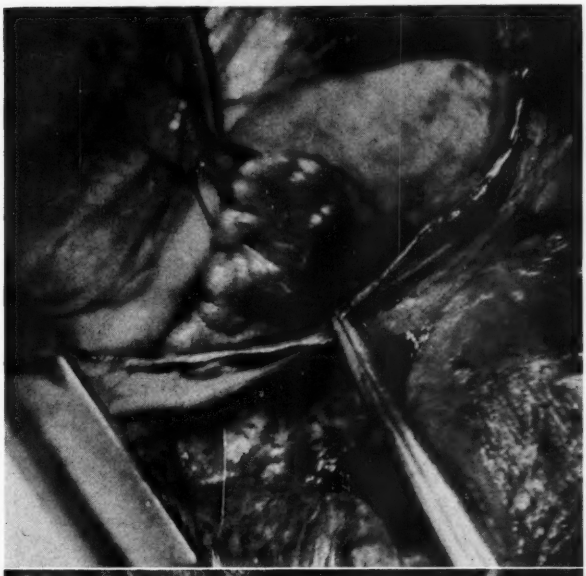

Fig. 4.

Fig. 5.

Fig. 4.—Distended auricular appendage protruding through incised pericardium.
Fig. 5.—Purse-string suture has been placed about the base of auricular appendage and temporary clamp applied.

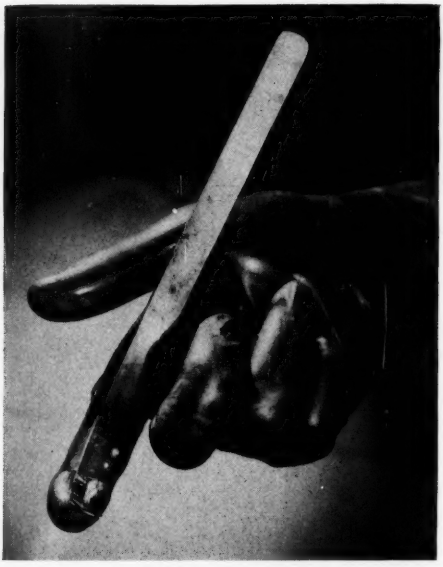

Fig. 6.—Commissurotomy knife inserted between two gloves on the palmar surface of the right index finger.

Fig. 7.—Right index finger and commissurotomy knife inserted through opening in left auricular appendage. Note handle of knife at upper center.

the cut on the medial side could be directed more posteriorly. Such a technique removes the necessity for the sheath with its extra bulk and the increased regurgitant blood loss which occurs between knife and sheath.

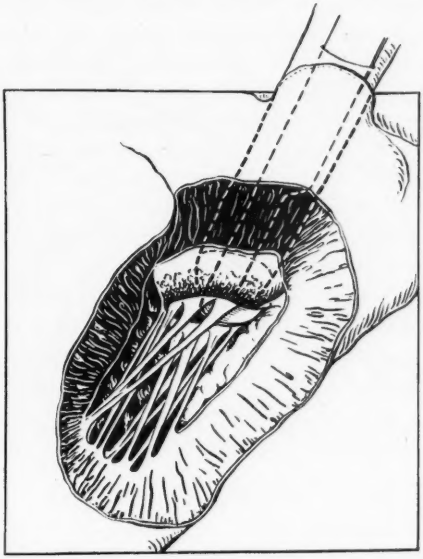

Fig. 8.—Tip of index finger at stenotic mitral orifice with hooked knife blade applied to anterolateral commissure.

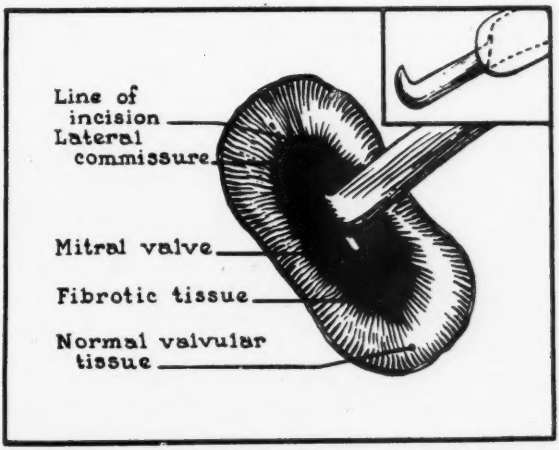

Fig. 9.—Diagrammatic representation depicting position of commissurotomy knife incising anterolateral commissure well into normal valve tissue.

We now, therefore, reinsert the knife through the orifice by simply pronating the hand, bringing the blade into apposition with the posteromedial commissure, which is then divided. In order to handle cases with a very hard or

calcified valve, we have prepared a special narrow-bladed backward-cutting punch (Fig. 10). This has a long bite so that it, too, will cut completely through the diseased tissue and into the flexible membranous valve. Thus we still obtain practically the same effect as by simple incision of the commissures but without the advantage of digital guidance. It is sometimes difficult accurately to delineate the commissures even by digital palpation. Blind palpation with an instrument inserted through the cardiac wall seems dreadfully inaccurate and inadequate. Perhaps some method of direct vision within the heart would be more advantageous. Allen and Graham[21] have devised a cardioscope with which the valve can be visualized with some accuracy. We have not had the advantage of this instrument. Until such an instrument becomes readily available and is of proved value, simple digital "vision" seems practical and adequate.

Having inserted the finger once more through the enlarged opening to make sure of its mobility and function, the finger and knife are deftly withdrawn from the auricle. The previously placed purse-string suture is drawn tight, preventing more than a few cubic centimeters blood loss. The suture is tied, and the cut edge of the appendage is oversewn (Fig. 11). There should be no disturbance of the systemic circulation and no irregularities throughout the procedure. The pericardium is left open and the pleura is drained. The chest wall is closed in layers.

Postoperatively, the patient may experience considerable pain for three to four days from the "chemical" pericarditis produced by manipulation. This is controlled by opiates. Ambulation is permitted within two to five days.

A word concerning the anesthetic methods employed may be in order at this point. The suggestions of Dr. Kenneth K. Keown, worked out in the departments of Dr. Frank Sèna at the Episcopal Hospital and Dr. Henry S. Ruth at Hahnemann Hospital, have been followed. Preoperative medication has consisted of nembutal or Seconal, gr. 1½, sixty to ninety minutes prior to the scheduled surgery; demerol, 75 to 150 mg., given thirty minutes later; and atropine sulfate, gr. 1/100 to 1/200, thirty minutes before induction. Intravenous procaine HCl in 0.2 per cent solution is begun fifteen minutes before sodium pentothal-curare induction. Oral intubation is carried out with this preparation, and procaine intravenous solution continued throughout the operation at the rate of 1 Gm. per hour for analgesia with additional sodium pentothal for hypnosis. High concentrations of oxygen are employed throughout. Nitrous oxide-oxygen (50%, 50%) for additional analgesia may be necessary. On this regime the patient is usually awake at the completion of surgery.

It is our present belief that commissurotomy by such a technique is a simple, relatively safe, direct method of re-establishing a normal type of valve function. It has the great advantage of direct digital guidance. It should not, and has not, in any of our four successful cases, produce any detectable amount of mitral regurgitation. Blood loss is minimal and no apparent disturbance to heart function results. That it effectively accomplishes the desired result is shown not only by the marked clinical improvement in all living patients, but also by objective physiologic studies. Thus, in a recent case (studied with the aid of

the Lilly electronic manometer) the pressures within the left auricle taken at the time of surgery fell from 45.2/30.3 mm. Hg (610/409 mm. H_2O) to 14.5/2.6 mm. Hg (195/35 mm. H_2O) fifteen minutes later (after commissurotomy). This interval had not been marked by blood loss (30 c.c.), cardiac arrhythmia, nor

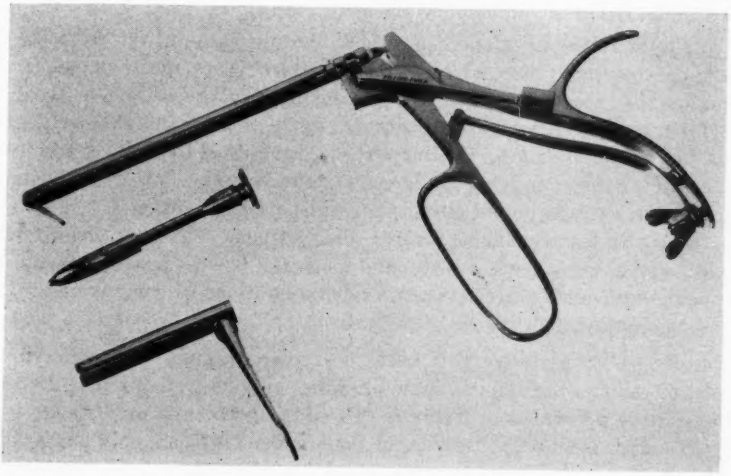

Fig. 10.—Narrow-bladed commissurotomy punch with trocar and cannula.

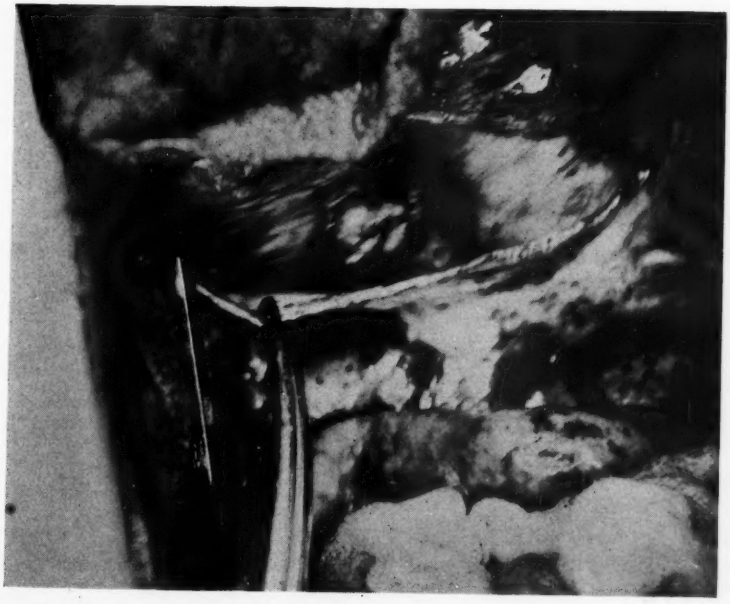

Fig. 11.—Auricular appendage ligated at base and oversewn at tip after commissurotomy.

blood pressure changes. Preoperative cardiac catheterization revealed the right auricular pressure to be 17.4/4.5 mm. Hg and a right ventricular pressure of 96.2/19.6 mm. Hg. We were technically unable to introduce the catheter into the pulmonary artery at this time. Six weeks after surgery, auricular pressures had fallen to 9.9/3.4 mm. Hg, 48.6/7.0 mm. Hg in the right ventricle, and 48.5/16.1 mm. Hg in the pulmonary artery (Case 14).

Long-term follow-up alone can supply the ultimate answer as to the effectiveness of commissurotomy. Nevertheless, since years must elapse for such information to become available, we feel justified in proceeding in those cases which meet our present rigid indications and in which it might be lifesaving. In this, our thinking follows the line already established by Blalock and Taussig with regard to their work on pulmonary stenosis. The day will undoubtedly come when an extracorporeal circulation will permit exclusion of the heart and lungs from active duty during intracardiac surgery. At that time it will be possible to open the heart widely and perform plastic procedures upon the valves and septa under direct vision. Such operations as commissurotomy will then become antiquated.

Results.—Our early results were most discouraging, but with improved selection of cases have begun to show promise. A summary of our entire experience to date is appended in Table I. In addition there is an abstract of each case. (See Case Reports.) Because of the number (fifteen), only a brief outline of each can be included in this presentation.

TABLE I. MITRAL STENOSIS

PATIENT	DATE OF OPERATION	TYPE OF OPERATION	RESULT
1. W. S.	11/14/45	Attempted valvulotomy	Death on table
2. W. S.	6/12/46	Digital dilatation	Death after 60 hours, thrombosis at valve site
3. W. W.	3/22/48	Commissurotomy	Death after 6 days, technical difficulty
4. J. R.	5/21/48	Exploratory	Death on table after pericardium incised
5. C. W.	6/10/48	Commissurotomy	Living, excellent result
6. S. S.	6/27/48	Commissurotomy	Living, excellent result
7. F. G.	7/13/48	Commissurotomy	Death after 7 days, sudden cerebral embolus
8. H. B.	8/ 2/48	Simple incision cusp	Death after 3 months, mitral regurgitation
9. J. K.	9/ 2/48	Simple incision cusp	Death after 24 hours, mitral regurgitation
10. A. W.	9/ 2/48	Commissurotomy	Death after 24 hours, hemorrhage
11. M. R.	9/10/48	Interauricular shunt	Death after 60 hours, diminished cardiac output
12. M. B.	9/16/48	Digital dilatation	Living, greatly improved
13. M. L.	2/ 1/49	Digital dilatation	Death after 60 hours, cardiac failure
14. J. B.	2/ 2/49	Commissurotomy	Living, excellent result
15. S. C.	3/23/49	Commissurotomy	Living, excellent result

CASE REPORTS

CASE 1.—W. S., a white man, aged 37 years, was admitted to Hahnemann Hospital on July 31, 1945, with the diagnosis of rheumatic heart disease with mitral stenosis. There was a history of many childhood diseases, including scarlet fever and acute rheumatic

fever at the age of 10 years, two previous grand mal seizures, and alcoholism. There were two previous hospital admissions—May 23, 1943, and Aug. 19, 1944—for cardiac decompensation. At this admission he complained of weakness, fatigue, repeated attacks of hemoptysis, and dyspnea, with precordial and epigastric pain. Physical examination revealed marked cardiac enlargement, apex beat in the sixth interspace anterior axillary line, totally irregular pulse rate of 110 with pulse deficit; at the apex, a diastolic murmur ending in a slapping first sound was heard. P_2 and A_2 were increased in intensity. There was auricular fibrillation, no precordial thrill, and blood pressure was 100/64. Dosage of digitalis was readjusted as the patient had not followed his digitalization program faithfully.

Routine laboratory studies were within normal range. Teleroentgenograms revealed marked enlargement to the right, moderate to the left, with marked indentation of the esophagus by the left auricle seen on lateral views. Chest x-ray examination for lung fields revealed chronic thickening of the root shadows but no extension beyond the hilar zone. Electrocardiograms confirmed the clinical finding of auricular fibrillation with myocardial degeneration. Venous pressures were slightly elevated, circulation time increased, especially arm to tongue; exercise tolerance diminished.

On Sept. 24, 1945, intercostal nerve block of the left first to fourth thoracic ganglia was performed with 1 per cent procaine and repeated with absolute alcohol after demonstration of some relief of anterior chest wall pain.

After considerable rest and care designed to improve his general condition, the patient was placed on preoperative penicillin and quinidine (to reduce cardiac irritability). On Nov. 14, 1945, mitral valve exploration was attempted under cyclopropane, oxygen, and ether endotracheal anesthesia. Coincident with the placing of purse-string sutures in the extremely friable auricular appendage, uncontrollable hemorrhage resulted and the patient died on the table despite all attempts to obtain hemostasis.

Case 2.—W. S., a white woman, aged 29 years, was admitted to Hahnemann Hospital, May 4, 1946, with the diagnosis of rheumatic heart disease with mitral stenosis. There was a history of scarlet fever and acute rheumatic fever at the age of 7 years. Since that time there had been many transient attacks of malaise and joint pains. In 1935, there was an onset of ankle and generalized edema. In 1939, congestive failure again developed during pregnancy. Therapeutic abortions were done in 1941 and 1944. She had been on and off digitalis therapy since 1935. On admission prior to surgery, the patient had a temperature elevation to 101° F., sore throat, and nausea. Râles were present in both lungs, as were edema of thighs, legs, and ankles, with ascites, liver edge felt 7 cm. below costal margin, and marked venous engorgement. The heart was regular in force, rate, and rhythm; pulse 92, blood pressure, 100/80. It was enlarged both to the right and the left; a diastolic murmur was present at the apex, P_2 was accentuated. Teleroentgenograms indicated most marked enlargement of the right heart border and to a lesser extent the left ventricle. The left auricle bulged into the esophagus. Routine laboratory studies were not unusual except for albumin in the urine. Electrocardiographic tracings showed a sinus rhythm with marked right axis deviation, deformed P waves in all leads, T waves flat in lead one, P-R interval .2 seconds.

The patient was given digitalis treatment, diuretics, analgesics, quinidine, vitamin K, and penicillin. There was marked improvement during the ensuing weeks. Immediately prior to surgery examination of the heart revealed a harsh presystolic mitral murmur with a sharp mitral first sound, a soft short systolic blow, P_2 greater than A_2, rate and rhythm regular. Exercise tolerance had improved but was not normal; circulation times and venous pressures had returned to normal. The patient was operated on June 12, 1946, and the mitral valve dilated manually. Originally a special backward-cutting punch had been inserted, but the mitral orifice could not be located with this instrument. The valve orifice was felt to split at both angles. Immediately following this maneuver the blood pressure rose to 130/80 and her general condition and circulation greatly improved. After reacting from anesthesia a grade 2 systolic blowing murmur was heard with a slight diastolic component. There was no accentuation of P_2. A biphasic friction rub was heard. Blood

pressure was 114/76, pulse 100, temperature 100.4° F. Improvement continued for forty-eight hours, when the patient went into sudden collapse, no pressure or pulse obtainable. There was marked dyspnea, heart sounds distant, moist râles throughout lungs, liver edge again down to the preoperative level. Therapeutic measures included pleural aspiration of 150 c.c. bloody serum, positive pressure oxygen mask, innumerable cardiac stimulants, but were of no avail. The patient died at 10:45 P.M., June 14, 1946.

Autopsy Findings.—

Heart: No antemortem thrombi in either the pulmonary artery or the left arterial appendage were found. There was dilatation of the right atrium, marked hypertrophy, and dilatation of the right ventricle, the right ventricular wall measuring 7 mm. in thickness; hypertrophy and dilatation of the left atrium, small-sized left ventricle. There was marked stenosis with calcification of the mitral ring, the ring admitting only the tip of one finger. At the commissures there was clotting and thrombosis in small slits which had been made by surgical finger dilatation. The remainder of the heart valves were relatively normal.

It was during this examination that the idea of more accurate incision of the commissures under direct palpation was formulated.

CASE 3.—W. W., a white man, aged 39 years, was admitted for the seventh time to The Memorial Hospital, Wilmington, Del., this time with the diagnosis of rheumatic heart disease with mitral stenosis. His previous admissions had been occasioned by repeated bouts of hemoptysis regarded to be on the basis of bronchiectasis. On these previous occasions he had had a variety of symptoms in addition to hemoptysis, such as fever, malaise, and chest pain, and chest x-ray examination had revealed transient areas of pneumonitis. Repeated bronchograms had shown cylindrical bronchiectasis of the medial basal division of the right lower lobe, which segment had been removed surgically on April 28, 1947. At the age of 14 years he had suffered an attack of acute rheumatic fever.

Examination of the heart at the time of this final admission revealed the presence of a grade 3 systolic murmur with a low-pitched rumbling diastolic murmur heard at the apex. The heart was compensated, electrocardiogram was normal except for sinus tachycardia, chest x-ray views revealed a mitral configuration; all other studies were within normal range.

Operation was performed on March 22, 1948, and was the first attempt at planned incisional commissurotomy in our hands. The right index finger was inserted through the left auricular appendage, and the mitral valve explored. A large fungus-like mass, roughly 1.5 cm. square, arose from the posteromedial commissure. This protruded into the mitral orifice, making it impossible to incise this commissure. The anterolateral commissure was partially cut and dilated by using an ordinary surgical scalpel on the index finger. This instrument was most unsatisfactory and necessitated a sawing motion at the commissure as it slid over the fibrotic angle. A cut of ⅜ inch was thought to have been made, plus vigorous dilatation of the valve ring. The necessity for a better cutting instrument obviously resulted from this experience and has led to the development of our present knife (Fig. 6).

Postoperatively the patient was heparinized, it being reasoned that this procedure might prevent the clotting or thrombosis which had occurred in Case 2. This proved to be disastrous, for excessive oozing ensued, requiring repeated pleural aspirations in addition to the usual intercostal drainage catheter. In addition, coincident with the administration of heparin, excessive amounts of fluids were given. The combination of an inadequately performed commissurotomy (autopsy finding), heparin, and an overloaded circulation produced heart failure, terminal pulmonary edema, and death six days after surgery.

CASE 4.—J. R., a white man, aged 29 years, was admitted to the Philadelphia General Hospital in May, 1948, with a diagnosis of advanced rheumatic heart disease. Acute rheumatic fever had developed at the age of 12 years. He was apparently well until May, 1947

(diagnosis of mitral stenosis made in the Army in 1943), when he became dyspneic and edematous. Digitalis and mercurial diuretics relieved his distress. There had been four subsequent hospital admissions for cardiac failure despite continuous digitalization. Thoracentesis at time of last admission yielded 1,500 c.c. Examination upon this final admission revealed mild orthopnea without cyanosis, basal râles in both lung fields, and enlargement of the liver to 19 cm. below the costal margin in the midline. There was no ascites or peripheral edema. Cardiac examination indicated generalized enlargement but a regular, although rapid, rate of 104. A grade 3+ systolic and low-pitched rumbling diastolic murmur was heard at the apex. P_2 was greatly accentuated.

Electrocardiographic tracings and cardiac x-ray pictures confirmed the advanced stage of this patient's heart disease. Venous pressures varied from 115 to 340 mm. of water over a three-week period; circulation times showed great delay from arm to tongue. Ballistocardiographic studies were unsatisfactory.

Surgery was attempted on May 21, 1948, although he was an extremely poor candidate. After incision of the pericardium, the slightest touch of the heart surface produced runs of premature contractions. Despite all known forms of medication, his cardiac hyperirritability increased, ventricular fibrillation developed, and death promptly ensued before intracardiac manipulation of the mitral valve could be attempted.

CASE 5.—C. W., a white woman, aged 24 years, was admitted to the Episcopal Hospital on May 13, 1948, with a diagnosis of rheumatic heart disease with mitral stenosis. Acute rheumatic fever had occurred at the age of 7 years, with no recurrences. Her condition was asymptomatic until 1946, although the presence of a heart murmur had been confirmed repeatedly before this time. In 1946 slowly progressive dyspnea developed, with increasingly frequent attacks of hemoptysis. Her family physician made the diagnosis of mitral stenosis. One attack of cardiac decompensation occurred, treated by digitalization and restricted activity. Despite this regime, dyspnea increased, she was unable to perform her housework or care for her child. On admission examination was relatively normal except for her heart, which was markedly enlarged, particularly the left auricle. There was normal sinus rhythm, a loud, rasping diastolic murmur at the apex, pulse 120, blood pressure 110/72. These findings were confirmed by x-ray examination and fluoroscopy of the heart and electrocardiogram. Routine laboratory studies were within normal limits, venous pressure 110 mm. of water, circulation time arm to lung 12 seconds, arm to tongue 20 seconds. She responded normally to the usual exercise tolerance tests. Ballistocardiographic studies indicated a resting cardiac output of 4.38 liters, which could be increased to 9 liters on exercise.

This patient was considered to be by far the best candidate for surgery whom we had seen to date. Preoperatively she was digitalized and quinidine was given. On June 10, 1948, she was subjected to commissurotomy, which proceeded according to the technique described in this paper without flaw. The anteromedial cusp only was incised. Postoperatively she improved rapidly and was discharged from the hospital on the seventh postoperative day. She returned six weeks later for repeat heart x-ray views and ballistocardiographic studies. The x-ray views revealed considerable reduction in the heart size, particularly of the left auricle. Ballistocardiographic tracings indicated the same resting cardiac output as was present preoperatively, but after exercise this was increased to 12.6 liters. Clinically her improvement, however, was much more marked than these objective findings. In the nine months since surgery she has assumed the entire care of her household and is living a perfectly normal life. Digitalis is now unnecessary.

CASE 6.—S. S., a white woman, aged 35 years, was admitted to the Episcopal Hospital in June, 1948, with a diagnosis of rheumatic heart disease. There was no history of rheumatic fever having occurred during childhood. Indeed, she was well until 1940, when an obstetrician made the diagnosis of a serious heart murmur during pregnancy. During the twelfth week of this pregnancy she developed signs of cardiac failure (cough, pulmonary edema, and shortness of breath), requiring confinement to bed until completion of

gestation. She was then reasonably well until 1946, when she experienced a splenic infarct. In September, 1947, a second splenic infarct occurred, followed in two weeks by a cerebral embolus, causing paralysis of the left side. Motor power completely returned, but she was stricken with a psychosis resembling catatonia. Since that time she has been emotionally unstable, and her speech is slurred. In April, 1948, there was an embolus lodged in the dorsalis pedis artery of the left foot. On admission, in addition to the residual findings of the previously mentioned vascular accidents, her heart was irregular in rate, rhythm, and force—apparently from auricular fibrillation. There was enlargement to the left and a short, rumbling diastolic murmur could be heard at the apex. Blood pressure was 110/80. There were no signs of cardiac decompensation.

Routine laboratory studies were within normal range. Electrocardiographic tracings indicated an auricular rate of 375 and a ventricular rate of 60, interpreted as auricular flutter and flutter fibrillation. Venous pressure, right arm, was 178 mm. water. Circulation time, arm to lung, 9 seconds; arm to tongue, 18 seconds. Fluoroscopy and cardiac x-ray views confirmed the impression of mitral stenosis with enlargement of the left auricle.

The patient was digitalized and penicillin was administered. Immediately before surgery she was given quinidine, gr. 3, every three hours.

Commissurotomy was performed on June 27, 1948. Both commissures were cut using the left- and right-cutting knives inserted through a metal sheath strapped to the index finger, as described in the text. The valve orifice was small and the valve structure similar to muslin. At the conclusion of the procedure the auricular appendage was ligated at its base to prevent further embolic phenomenon.

Postoperative recovery was smooth and without incident. There has been marked clinical improvement, definite diminution in the size of the heart shown by fluoroscopy and cardiac x-ray view. Ballistocardiographic estimations of cardiac output at rest and exercise taken pre- and postoperatively indicate considerable objective improvement.

CASE 7.—F. G., a white woman, aged 35 years, was admitted to the Episcopal Hospital on July 1, 1948, with a diagnosis of rheumatic heart disease. Although there was no definite attack of acute rheumatic fever during childhood, she had repeated bouts throughout her life of epistaxis, and aching in the elbows, ankles, and wrists. She stated that she had always been short of breath. In 1925, during pregnancy, the presence of a heart murmur was discovered. Shortly thereafter, severe hemoptysis occurred and she was bedridden for five months. She underwent cesarean section at term. In 1927 she became pregnant for the second time with a return of the symptoms, at which time she underwent hysterectomy. In 1945 she was hospitalized for cardiac failure. Since that time she has had precordial pain, burning with radiation down both arms, and slight ankle edema.

On admission the patient was mildly dyspneic at rest, and could not walk the length of the corridor without severe dyspnea. She was taking digitalis, gr. 3 daily. Electrocardiographic tracings indicated a ventricular rate of 80 with auricular fibrillation. Cardiac examination showed cardiac enlargement to the left and a diastolic murmur over the apex. Lungs were clear; there was no enlargement of the liver nor peripheral edema. Venous pressure, right arm, was 120 mm. water; circulation time, arm to tongue, 27 seconds. Blood pressure was 120/80. Cardiac x-ray views were compatible with the diagnosis of mitral stenosis.

Commissurotomy was performed on July 13, 1948, in the classical manner. Exploration of the mitral valve revealed the mitral orifice to be too small to permit the insertion of the finger tip. It felt like a buttonhole in a piece of kidskin. The anterolateral commissure was satisfactorily incised and the thrill which was very prominent in the region of the mitral valve disappeared. It was deemed unnecessary to cut the posteromedial commissure. Transfixion sutures of medium cotton are placed through the tip of the auricular appendage and hemostasis was well established. The patient did exceedingly well postoperatively, and was able to traverse the halls with considerably more facility than she could preoperatively, as early as the sixth postoperative day. On the eighth postoperative day, while sitting up in bed talking to her husband, she died suddenly.

Autopsy Findings.—

Heart: A small antemortem thrombus was found in the stump of the amputated (partially) left auricular appendage. The sutures used for this closure were not exposed within the left atrium. The mitral valve appeared patent and the incision in the commissure showed no signs of fibrosis.

Brain: There was generalized edema of the brain, although the vessels did not appear markedly congested. There was a cone-shaped impression on the medulla and the base of the cerebellum, indicating herniation through the foramen magnum. On section of the cerebellum, there was a very definite area of softening, about 2 to 3 cm. in diameter, in the midportion. No obvious hemorrhage in this area was seen.

CASE 8.—H. B., a white man, aged 35 years, was admitted to The Memorial Hospital, Wilmington, Del., on July 22, 1948, with a diagnosis of rheumatic heart disease. There was a history of acute rheumatic fever in 1942. Since that time he has been admitted to the hospital on six occasions prior to the present admission for symptoms of increasing shortness of breath, hemoptysis, and edema. At the time of the present admission, although he was taking digitalis routinely his complaints were that of cardiac decompensation. Physical examination at this time revealed a heart enlarged to the left, normal sinus rhythm, no palpable thrill, marked crescendo, presystolic murmur heard at the apex. There was no sign of pulmonary or peripheral edema; venous pressures were normal as were the circulation times. Cardiac x-ray views were compatible with the diagnosis of mitral stenosis. After a period of care during which the patient received parenteral penicillin, an increased dosage of digitalis, and the institution of quinidine, he was referred for mitral valve surgery.

On Aug. 2, 1948, mitral commissurotomy was attempted. Exploration of the valve revealed the orifice to be very tiny, almost pinhole in type. Because of the marked constriction, no actual commissures could be located. Therefore, the anterolateral cusp was incised in the area assumed to be the general location of the anterolateral commissure. The opening so produced seemed very adequate, so that no further incision was attempted. Postoperatively the patient improved slowly, and there was evidence of a small amount of pulmonary edema. Electrocardiographic tracings showed that a definite change had occurred, in that there was more depression of the S-T segments in the chest leads with low voltage of the T waves in all leads. Clinically the preoperative diastolic murmur was absent and only a slight systolic murmur could be heard. By the ninth postoperative day the patient was out of bed without dyspnea, although fine râles could be heard in both lungs. The patient was discharged in satisfactory condition on Aug. 27, 1948.

He was re-admitted in October, when he was seized with severe chest pain and dyspnea. Physical examination revealed a cyanotic, dyspneic, apprehensive patient, exhibiting pitting edema of both ankles. Cardiac examination indicated that there were two murmurs heard at the apex, one systolic and one diastolic. Although there was some response to mercurial diuretics, there was progressive edema and the patient died in extreme heart failure on Oct. 18, 1948.

Autopsy Findings.—

Heart: The mitral valve was the seat of an operative incision 1 cm. in depth on the lateral aspect of the aortic cusp. There was no evidence of healing of this incision. There were additional calcareous deposits over the surface of the mitral valve.

CASE 9.—J. K., a white man, aged 31 years, was admitted to the Episcopal Hospital on Aug. 20, 1948, with a diagnosis of rheumatic heart disease. He had suffered an attack of acute rheumatic fever at the age of 12 years. After prolonged illness he recovered, and seemed well. In 1940 he passed the Army physical examination and was inducted. In 1943 he experienced repeated episodes of hemoptysis during exercise. At this time he was digitalized, and has remained so to the present admission. History to this time consists essentially of repeated attacks of hemoptysis, increasing shortness of breath, chest pain during paroxysms of coughing, but no peripheral edema. Examination on admission

revealed a patient in no acute distress, but one who became dyspneic while talking. Cardiac examination revealed moderate enlargement, normal sinus rhythm with occasional premature contractions, accentuated P_2, and a snapping M_1. There was a rumbling murmur throughout diastole, with presystolic accentuation. There were no signs of congestive failure. Circulation time was, arm to tongue, 19 seconds; arm to lung, 6 seconds. Venous pressure was 160 mm. water. Electrocardiogram revealed a right axis deviation. Cardiac x-ray views were compatible with the diagnosis of mitral stenosis, showing marked left auricular hypertrophy.

Mitral commissurotomy was performed on Sept. 2, 1948, in the classical manner. Mitral exploration revealed a tight fishmouth constriction of the valve orifice. Both lateral and medial commissures were incised. Because of the presence of hard, calcified nodules along the medial commissure, the angle of the medial incision was directed slightly anterior, and a large incision was produced.

The patient responded well immediately after surgery, but during the night began to expectorate frothy, bloody sputum. His course was progressively downward despite all therapeutic endeavor, and he died the next day in acute pulmonary edema.

Autopsy Findings.—

Heart: The mitral leaflets are thickened, rigid, and calcified. The chordae tendineae are shortened and cordlike. There is stenosis of the ring and regurgitation. The latter has been accentuated by surgical incision, which has been carried into the intracardiac portion of the aorta.

CASE 10.—A. W., a white woman, aged 35 years, was admitted to the Episcopal Hospital on Aug. 27, 1948, with a diagnosis of rheumatic heart disease. There was no previous history of rheumatic fever. At the age of 26 years, during her first and only pregnancy, she experienced episodes of marked dyspnea and orthopnea with peripheral edema and precordial pain. The patient's pregnancy was terminated by cesarean section. The subsequent course was that of increasing progressive dyspnea, but no hemoptysis occurred. The patient has been digitalized for several years. Physical examination revealed blood pressure 120/78, pulse 76, cardiac enlargement to the left, P_2 accentuated 2+, diastolic thrill at the apex, rumbling apical diastolic murmur, ending in a snapping M_1. The lungs were clear, the liver and spleen not palpable.

Preoperative studies included fluoroscopy, cardiac x-ray views, and electrocardiogram which revealed right axis deviation; circulation time with Decholin was 18 seconds, with ether 7 seconds. Venous pressure was 120 mm. water in the right arm. The preoperative preparation included quinidine and penicillin, in addition to the usual care.

Mitral commissurotomy was performed on Sept. 2, 1948. A typical fishmouth fibrotic mitral valve was encountered. Both the lateral and the medial commissures were cut as in the preceding case. Immediately after the medial commissure was incised, the blood pressure dropped markedly and the heartbeat became slow and feeble. This was believed to be due to the loss of an excessive amount of blood through the sheath of the commissurotomy knife inadvertently. The blood was rapidly replaced, with improvement of her condition. The base of the appendage was ligated but no end sutures were placed in the amputated tip of the appendage.

As in the preceding case, the immediate postoperative condition was good, but after twelve hours the blood pressure dropped steadily and despite all therapeutic endeavor the patient died within a twenty-four-hour period. Attempts at cardiac resuscitation by manual massage in bed were to no avail. During this procedure it was noted that considerable hemorrhage had occurred from the stump of the auricular appendage.

This case indicated to us the necessity for both ligation of the base of the appendage and suture of the amputated appendageal tip. These last two cases emphasized to us the undesirability of the sheath which we had been using to facilitate the use of a left- and right-cutting commissurotomy knife. We are grateful to Harken for his suggestions as noted in the text, which have made it possible to dispense with this sheath.

No autopsy was obtained.

CASE 11.—M. R., a white woman, aged 43 years, was admitted to the Episcopal Hospital in September, 1948, with the diagnosis of rheumatic heart disease. There was no history of acute rheumatic fever, but the presence of a heart murmur had been detected in 1930 at the time of examination for life insurance. At the age of 25 years, during her first and only pregnancy, she collapsed from a "heart attack," and the fetus was delivered by cesarean section. At the age of 38 years she experienced a sore throat with fever, which was diagnosed as an attack of rheumatic fever. At the age of 41 years there was cerebral embolization, which affected her speech, the effect lasting for one week. Several months later a second embolus occurred to the right leg, which cleared shortly. In 1947, splenic infarction occurred. The patient had never been in congestive failure, but took .2 mg. digitalis daily for four years. She had taken Dicoumarol, 37.5 mg. daily, since August, 1947.

Physical examination revealed an enlarged heart, auricular fibrillation, marked diastolic mitral murmur, and blood pressure 110/80. There were basal râles in the lung fields, but no other signs of congestive failure.

Fig. 12.—Forceps in interauricular septal defect produced surgically. Note large size compared to stenotic mitral orifice.

Preoperative studies included fluoroscopy and cardiac x-ray examination confirming the diagnosis of mitral stenosis. Venous pressure was 160 mm. water, circulation time, arm to lung, 3 seconds; arm to tongue, 16 seconds. Electrocardiographic studies indicated ventricular rate of 80 with auricular fibrillation and right axis deviation.

Mitral exploration was carried out Sept. 10, 1948. A tiny mitral orifice was found high on the anterior aspect of the mitral valve and was in such a position that commissurotomy could not be performed. Exploration of the interauricular septum was carried out. This revealed a semilunar ridge, somewhat simulating a valve. The commissurotomy knife was engaged upon the tissue proximal to this ridge and an opening was made into the adjacent chamber (right auricle). This opening was then enlarged by two separate diverging strokes of the knife to fashion an interauricular septal defect which would admit

the index finger. Postoperatively the patient responded adequately and remained clear and lucid until death sixty hours later, despite systolic blood pressure ranging from 40 to 60 mm. mercury. All attempts to elevate and sustain a higher blood pressure failed. Oliguria and terminal uremia followed. Our attempts to relieve pulmonary hypertension had so lowered this patient's cardiac output that life could not be maintained. The heart is shown in Fig. 12.

CASE 12.—M. B., a white woman, aged 37 years, was admitted to the Episcopal Hospital on Sept. 7, 1948, with a diagnosis of rheumatic heart disease. She had experienced an attack of acute rheumatic fever at the age of 14 years, with four recurrent attacks after that time. She had been taking digitalis continuously since the first attack. There had been three episodes of marked dyspnea, occurring during pregnancy sixteen years ago, the next in October, 1947, and the third in July, 1948. Edema of the ankles occurred on two occasions, one at the birth of her child sixteen years ago, and again in July, 1948. There was marked exertional dyspnea, but she was able to work with care up to the time of admission.

Physical examination revealed enlarged heart, both to the right and to the left, auricular fibrillation, marked systolic murmur at the apex, with an early diastolic thrill and murmur in the same area. After the usual studies, it was felt that this patient had mitral stenosis and regurgitation of equal severity, and the problem arose as to whether surgery in her case was indicated. Cardiac catheterization studies were unsatisfactory. After consultation with the cardiologist, it was our combined opinion that this patient's course would be rapidly downhill at best, and therefore an attempt at mitral exploration and relief of stenosis was indicated.

Mitral exploration was carried out on Sept. 16, 1948. The mitral valve was found to be very abnormal. The medial half was apparently occupied by a large calcified mass, which was notched at the exact commissure. It was evident that no operation could be performed on this portion of the valve. The lateral half, however, was widely dilated so that the palpating finger could easily be inserted into the left ventricle, even to the apex. The edge of this opening was fibrotic and there was little movement of the valve during cardiac excursion. An attempt was made manually to split and mobilize this stiffened lateral wall, feeling that possibly some motion in the valve might result in improvement. Nothing further was done.

Postoperatively, to our amazement, she has been markedly improved subjectively, although there are no objective findings to corroborate such improvement. There was a marked psychic element in this case which might account for this improvement.

CASE 13.—M. L., a white woman, aged 53 years, was admitted to Doctors Hospital, Philadelphia, on Jan. 16, 1949, with a diagnosis of rheumatic heart disease. Acute rheumatic fever had been sustained three times between the ages of 7 and 10 years. Since the age of 43 years she has had repeated attacks of congestive failure. Physical examination revealed a thin, emaciated woman, prominent neck veins, liver enlarged to 3 cm. below costal margin, moderate ascites, and grade 2 pitting pre-tibial edema. Examination of the heart revealed a loud, blowing diastolic murmur, cardiac enlargement, evidence of auricular fibrillation. There were râles at both bases posteriorly.

Preoperative studies included electrocardiographic tracings indicating auricular flutter; cardiac x-ray views gave evidence of mitral configuration with left auricular and ventricular enlargement confirmed by fluoroscopy. Venous pressure was 120 mm. water; circulation time, arm to lung, 9 seconds; arm to tongue, 27 seconds. Cardiac catheterization was performed and pressure readings in the pulmonary artery were 32.4 systolic and 3.4 diastolic. In the right ventricle pressure readings of 62.3 systolic and 7.6 diastolic were obtained.

It seemed unlikely that surgery was indicated in this case, but at the behest of the patient and the cardiologist who realized the hopelessness of the situation, operative intervention was carried out. Mitral exploration was performed on Feb. 1, 1949. The auricular appendage was found to be tightly adherent to the pericardium and the entire pericardial

space was obliterated by fibrous adhesions. As the auricle and its appendage could not be freed, mattress sutures were placed circularly in the auricular appendage. An incision was made through this area and the finger inserted into the left auricle. The mitral valve was found to be a fibrotic slit somewhat wider anteriorly than posteriorly. The index finger was inserted through the orifice of the valve, which was manually dilated. Tearing at both commissures was accomplished. The finger was withdrawn, and the mattress sutures were drawn tight. This did not suffice to control the bleeding, and a large-sized gelfoam pack was applied over the rent in the auricular appendage. The pericardium was sutured over the area and bleeding was very adequately controlled.

The postoperative period was one of progressive cardiac failure, despite intensive therapy. The patient died within sixty hours.

Autopsy Findings.—

Heart: There was an adhesive pericarditis with multiple calcium deposits, and severe mitral and aortic stenosis, the former being the seat of lacerations at the commissures. Both ventricles were markedly hypertrophied. All other organs were the seat of marked passive congestion.

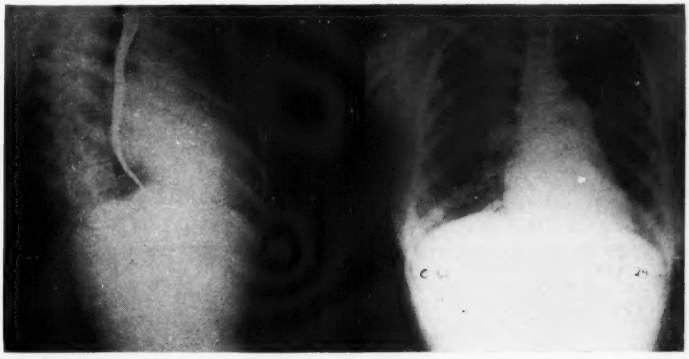

Fig. 13.—Posteroanterior and right anterior oblique roentgenograms showing size of heart and left auricle, preoperative.

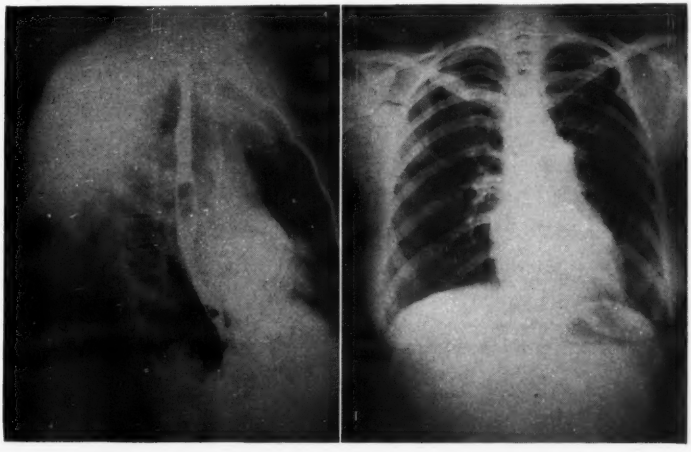

Fig. 14.—Posteroanterior and right anterior oblique roentgenograms showing reduced size of heart and left auricle, postoperative.

CASE 14.—J. B., a white man, aged 32 years, was admitted to the Hahnemann Hospital on Jan. 18, 1949, with the diagnosis of rheumatic heart disease. To the patient's knowledge there was no history of acute rheumatic fever. The patient had noticed increasing dyspnea since 1945, with four episodes of marked hemoptysis. In recent months dyspnea was marked on the slightest exertion. There was no history of congestive failure. Marked cardiac palpitations, but no anginal or substernal pain, were present.

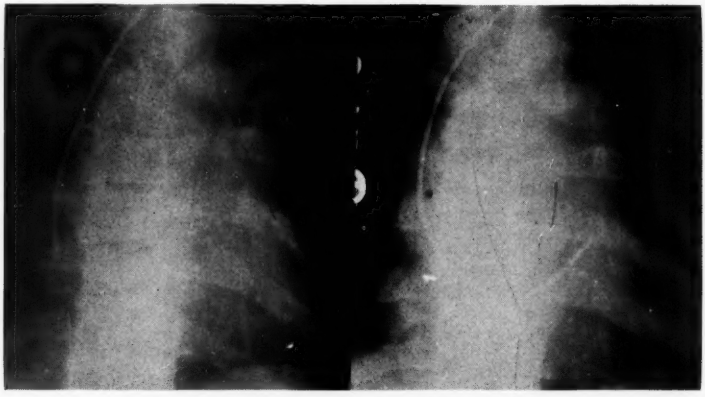

Fig. 15.—Position of catheter in right auricle and ventricle at the time of postoperative pressure studies (Case 14).

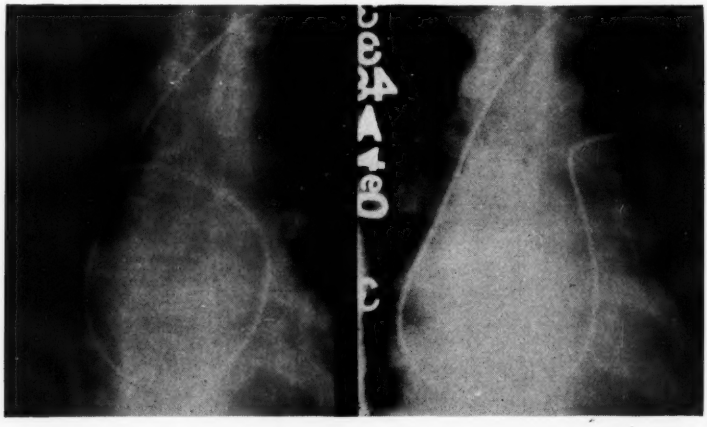

Fig. 16.—Position of catheter in right and left pulmonary arteries at time of postoperative pressure studies (Case 14).

Physical examination of the heart revealed a normal sinus rhythm, early diastolic murmur at the apex, P_2 accentuated, and blood pressure 110/60. Fluoroscopy and teleroentgenograms indicate cardiac enlargement with mitral configuration. Electrocardiographic tracings indicate some auricular dysfunction and myocardial damage with slight right axis deviation. T waves are inverted in Lead CF_2. P waves are of abnormal duration in Lead 2. Routine laboratory studies were within normal limits. Venous pressure for the right arm was 120 mm. water. Circulation time, arm to lung, was 10 seconds; arm to tongue, 22 seconds. Preoperative cardiac catheterization findings are contained in the text.

Mitral commissurotomy was performed on Feb. 2, 1949, and the mitral slit was found to be so small that it would not admit more than the tip of the finger. The edges of the mitral orifice were folded and beaded. There was a small piece of calcium high on the anterior leaf. The remainder of the mitral valve, both anterior and posterior leafs, was thin and mobile. The lateral commissure was slit by a backward stroke of the commissurotomy knife, and the commissure was divided laterally to the wall of the heart. The opening so produced was large and adequate, and it was felt that medial commissurotomy was unnecessary.

Postoperatively the patient's course was excellent, except for the occurrence of more than the average amount of pericardial pain, which disappeared after one week. The patient was discharged and returned on Feb. 28, 1949, for complete postoperative studies. During this admission, auricular fibrillation came on suddenly, but he reverted to normal rhythm on digitalis and quinidine, which was then discontinued. Venous pressures in the right arm were 95 and 100 mm. water; circulation times, arm to lung, 11 seconds; arm to tongue, 17 seconds. Postoperative catheterization studies (Figs. 15 and 16) as well as pressure readings in the left auricle, before and after commissurotomy, are contained in the text. All pressure readings were recorded on this and other catheterization study cases by a Lilly electronic manometer calibrated in millimeters of Hg. The patient has since returned to work and is now able to carry on the duties (strenuous) of a truck driver in the coal mines.

CASE 15.—S. C., a white man, aged 21 years, was admitted to the Hahnemann Hospital on March 17, 1949, with the diagnosis of rheumatic heart disease. There was no history of acute rheumatic fever, but he was told on routine physical examinations at school and in the Army that he had a "rheumatic heart." He had been repeatedly warned to stay away from strenuous sports, a warning which he had ignored until recently, when he began to notice some slight shortness of breath on exercise. He was a sensitive youth and very heart-conscious. There were no other symptoms to date.

Cardiac examination revealed slight enlargement, normal sinus rhythm, and grade 3 rough diastolic murmur at the apex. There was no associated evidence of any tendency to cardiac decompensation.

Preoperative studies included electrocardiographic tracings which were within normal limits, fluoroscopy, and cardiac x-ray views which revealed very early mitral configuration. Venous pressures in the right arm were 140 mm. water, circulation time, arm to lung, 8 seconds; arm to tongue, 11 seconds. Cardiac output studies determined on the Fick principle indicated a cardiac output of 6.3 liters (cardiac index 3.9) before exercise and 13.5 liters (cardiac index 8.2) after exercise. These figures were not corrected for his preoperative anemia. Complete cardiac catheterization pressure studies were carried out and found to be as follows: Right auricle—maximum systolic 11.9 mm. Hg, maximum diastolic 3.5 mm. Hg; right ventricle—maximum systolic 37.8 mm. Hg, minimum systolic 30.7; maximum diastolic 5.4 mm. Hg, minimum diastolic 0.8 mm. Hg; right pulmonary artery—maximum systolic, 43.5 mm. Hg, minimum systolic 37.0; maximum diastolic 5.2 mm. Hg, minimum diastolic –0.6 mm. Hg. In the main pulmonary artery, maximum systolic, 52.5 mm. Hg, minimum systolic 42.1 mm. Hg; maximum diastolic 4.5 mm. Hg, minimum diastolic –3.4 mm. Hg. The heart rate during these studies varied between 78 and 84 beats per minute. On the basis of these studies, our cardiac consultant stated, "Even though there is no history of rheumatic infection, it is felt that this is a clear-cut case of advanced mitral stenosis. The pulmonic second sound is only 1+ accentuated, and there is no left ventricular enlargement. An exercise tolerance test gave a good response. This case should be a good candidate for commissurotomy, and I see no contraindication to its being done."

Mitral commissurotomy was performed on March 23, 1949, and a valve similar to that described in Case 14 but with a slightly larger orifice was found. Lateral commissurotomy was sufficient to obtain the desired result. During the performance of this operation, pressure readings were obtained before and after commissurotomy from the left auricle. Because of mechanical difficulties in the performance of our electronic manometer,

the readings obtained were unsatisfactory and inaccurate. Objective evidence to corroborate his marked clinical improvement will be obtained in one month from the time of operation, and will be reported at a later date.

Two cases were exploratory or attempted valve operations only, for both patients died before the heart was entered. In the first patient, operated upon Nov. 14, 1945, countertraction on sutures in the left auricular appendage during insertion of a trocar resulted in tearing of the appendage (Case 1). Fatal hemorrhage resulted. The second operation (Case 4) was attempted upon a man in extremely poor condition, who remained cyanotic from the onset of anesthesia. After the pericardium was opened the slightest irritation of the epicardium produced runs of premature contractions. In spite of vigorous intravenous drug therapy designed to reduce cardiac irritability, the heart failed. Drastic resuscitative measures were to no avail.

In two cases a technical error occurred, related to the use of a special metal sheath for the change of knife blades. In both, an incision was inadvertently made across the anteromedial valve cusp rather than through the posterior commissure. Both patients developed severe mitral regurgitation. One died within twenty-four hours and the other within three months (Cases 8 and 9).

In one case an interauricular shunt was produced (Fig. 12). The pulmonary and left auricular hypertension were promptly and adequately relieved. In fact, even the pre-existing auricular fibrillation was abolished. The patient, however, died within three days because she could maintain a systolic blood pressure of only 30 to 60 mm. mercury. By removing the auricular hypertension the compensatory head of pressure necessary to maintain adequate cardiac output had been so lowered that life could not be sustained (Case 11).

In three cases (Cases 2, 12 and 13) simple digital dilatation of the mitral orifice was carried out. Except for the first case (W. S., June, 1946) in which we had no clear-cut ideas of procedure other than to enlarge the stenotic valve, the indication for this procedure rather than commissurotomy was entirely based upon the poor condition of the patient at the time of surgery. In both, the simplest and most rapid procedure seemed advisable. One patient recovered (Case 12) and is, subjectively, remarkably improved. The proper pre- and postoperative set-up for physiologic studies was not available at that time, much to our regret. With our present knowledge none of these cases would have been considered for surgical intervention.

Commissurotomy by the technique described was performed in seven cases with three fatalities. In the first of these latter (Case 3) a modified scalpel was employed, as our present commissurotomy knife had not been perfected. Attempts to incise the commissure were attended by repeated disengagement of the blade as it rode over the fibrotic valve, resulting in an inadequate incision extending only a few millimeters into the scar tissue. Pre- and postoperative pressure determinations in the left auricle were unchanged (320 mm. H_2O). The patient died on the sixth postoperative day in pulmonary edema from unrelieved mitral stenosis. The second patient (Case 7) was operated upon accurately and well, and appeared to be on the way to a most satisfactory result, but suffered a cerebral embolus and died suddenly on the seventh postoperative

day. Autopsy disclosed an adequate and satisfactory commissurotomy. Thrombus formation had occurred in the left auricular appendage, from which the embolus apparently originated. We have observed such thrombus formation many times in animal appendages after valve surgery, but no adverse complications had resulted. We had simply oversewn the incision in the appendage at the conclusion of the procedure. In six succeeding cases (and in one previous, C. W.) we have ligated the auricular appendage at its base to prevent such disaster. The appendage of the third patient operated upon shortly thereafter was ligated at its base without suture of the cut tip. Autopsy indicated that hemorrhage had occurred from this site (Case 10). This experience has led to both ligation at the base and an oversewing suture at the cut tip on all subsequent cases.

The remaining four cases had excellent results. The patients are clinically well. The two patients who had been digitalized for some months prior to surgery no longer need such medication. There is denfiite diminution in the size of the heart as shown roentgenographically (Figs. 13 and 14). Their tolerance for exercise is remarkably increased, permitting them to return to normal activity. Careful examination has revealed some slight evidence of residual mitral stenosis (by auscultation) in two of the cases (Cases 5 and 14). The others seem to have no residual signs of the disease, although they are admittedly short-term follow-ups. There has been *no evidence of mitral regurgitation* in any of the four.

Comment.—It is essential that these patients be carefully studied and selected for surgery. This should include complete fluoroscopic examination of the heart, posteroanterior and oblique x-ray views including esophagograms, electrocardiographic tracings and phonographic recordings, circulation times, and venous pressures. A careful clinical history and examination are made by an especially interested cardiologist. Catheterization of the right heart is of utmost importance. Pre- and postoperative pressure readings from the pulmonary arteries, right ventricle, and auricle are at present the best objective means of evaluating the results obtained. In certain cases, angiocardiography to determine the size of the left ventricle may be indicated. Ballistocardiograms and cardiac output studies are of great value.

Indications (at present).—

1. Most favorable group:
   - A. Excessive fatigability.
     Increasing exertional dyspnea.
   - B. No rheumatic activity.
     Normal sinus rhythm.
     Lesion predominantly stenosis.
     Evidence of significantly increased pulmonary hypertension.
2. Less favorable group:
   The preceding plus:
   - A. Recurrent bouts of hemoptysis.
   - B. Arterial embolic phenomena.
   - C. Auricular fibrillation without failure.

Hemoptysis in more than amounts necessary to stain the sputum is of grave import. Wolff and Levine[22] pointed out that, in their series of cases, the average duration of life following the onset of severe hemoptysis is 32.5 months. Levine[23] stated that the average duration of life following the initial attack of congestive failure is 4.6 years. The development of auricular fibrillation is usually permanent and irreversible. In this state, thrombus formation not infrequently occurs along the endocardium of the dilated and relatively immobile auricular walls. Some 75 per cent of these occur within the lumen of the auricular appendage (left), a common site for the origin of arterial embolization.

Contraindications (at present).—

1. Active rheumatic infection.
2. Presence of superimposed subacute bacterial endocarditis.
3. Cardiac failure uncontrollable by medical means.
4. Presence of marked associated mitral regurgitation or other valve (aortic) deformities.

SUMMARY

Our entire experience with surgery for mitral stenosis—fifteen cases—has been reviewed. In seven of them, commissurotomy was performed with four excellent results and three deaths. Had our present knowledge been applied to all cases, the mortality would have been appreciably lowered.

Commissurotomy is a simple, direct, effective, and safe procedure. Its exact surgical technique has been outlined. It accomplishes relief of mitral stenosis by restoring valve function without the production of additional mitral regurgitation.

Digital guidance in the performance of accurate valve surgery is essential until a method of direct vision becomes established. The left auricular appendage is the most satisfactory avenue of approach to the mitral valve. The auricular appendage must be ligated at the conclusion of the procedure to prevent arterial embolization. This may prove to be the proper approach to the management of arterial embolization in many cases unassociated with mitral stenosis.

An enlarged left ventricle in a case of supposed "pure" mitral stenosis is indicative of some additional significant valve lesion (aortic stenosis or regurgitation or mitral regurgitation) and is probably contraindicative to commissurotomy.

Study methods of valve, in addition to clinical evaluation, embrace cardiac catheterization for determination of pulmonary vascular pressures, ballistocardiography, and other physiologic studies for the determination of cardiac output.

Venous shunts for the treatment of mitral stenosis are of some value, although their eventual effects upon cardiac output, the right ventricle, and the lesser circulation must be kept clearly in mind.

Since this paper was submitted for publication, seven additional mitral commissurotomies have been performed with but one death. Thus of fourteen patients with mitral commissurotomies to date, ten are living and have shown great improvement, both by subjective and objective measurements. Complete data on these additional cases will be presented in a later communication.

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DISCUSSION ON "THE SURGICAL TREATMENT OF MITRAL STENOSIS" BY DR. DWIGHT E. HARKEN, DR. LAURENCE B. ELLIS, AND DR. LEONA R. NORMAN;* AND "THE SURGERY OF MITRAL STENOSIS" BY DR. CHARLES P. BAILEY, DR. ROBERT P. GLOVER, AND DR. THOMAS J. E. O'NEILL

DR. RICHARD H. SWEET, Boston.—I have a suggestion to make, referred to by Dr. Bailey, on a procedure which might be of some interest to those of us who have not yet perfected our technique for intracardiac surgery, and I might add that, so far as I am concerned, I am going to wait for Dr. Harken and Dr. Bailey to do that before I start myself.

(Slides.) This operation is an attempt to reproduce outside the heart the physiologic effect of an interauricular septal defect. The diagram on this slide shows what we have done. Before this work was done, Dr. Bland of our Department of Cardiology suggested that in cases of tight mitral stenosis an extracardiac shunt between the pulmonary and the systemic venous systems might provide a sufficient release of pressure to relieve the congested pulmonary circulation.

This slide shows the anatomic findings at the operation on one of the patients. Here is the superior segment of the right lower lobe and at this point can be seen the superior

*See page 1 for article by Harken, Ellis, and Norman.

segmental branch of the inferior pulmonary vein. In this slide, drawn from the same operation after further dissection, there is as you see a small anomalous vein which lies somewhat above the superior segmental vein. In all the patients whom we have operated upon to date the diameter of the superior segmental vein has been equal to that of the azygos vein. My reason for using the nonsuture anastomosis technique is that the vessels are fragile, and it is my opinion that a suture anastomosis might be difficult and not as satisfactory from the functional point of view. At the completion of the operation in this case there was a rush of blood through the anastomosis into the azygos vein and a definite thrill could be felt. There was also a definite drop in the interauricular pressure from 530 mm. of water before the anastomosis was made to 379 mm. of water after the anastomosis was made.

Three of the patients have been enormously improved as a result of the operation. Each of these was formerly committed to a chair and bed existence but now leads an essentially normal existence. The fourth patient's operation was too recent for evaluation of the result. In the fifth case the patient died.

Dr. Harken was searching in his own mind for some objective evidence of striking relief—perhaps we should not call it cure—and I have discovered perhaps the test which he needs. Two of my patients before operation were unable to indulge in sexual intercourse without suffering pulmonary edema, and afterward everything was all right.

DR. A. J. GRACE, London, Ontario.—I have listened spellbound to this presentation by both our colleagues and by Dr. Sweet, who has done excellent work in this as well as other fields. The subject has interested Dr. L. D. Wilcox and myself in London for some years. We also have done a number of experiments on dogs such as have been mentioned. Perhaps two or three points might be mentioned very briefly. In the first place, this work confirms the principles Dr. Harken has given; they are very sound and, I think, in the main basic. One point we might add is that any damage done to one or more chordae tendineae in these operations is likely to lead very rapidly to cardiac dilatation and death within twenty-four hours in most cases. I think that point should be stressed. In all surgical work we seek to avoid adding to the damage and the risks as well as actually contributing to the health of the individual.

One point with regard to pressure changes: Immediately following section of a cusp of the mitral valve the pressure in the auricle rises very rapidly, as Dr. Harken has emphasized, and that provides mechanical problems and an extra danger of bleeding. It is rather amazing how slowly the rise appears in the pulmonary arterial side when records are kept, and how slight it is. Turning to the problem in man: we are dealing with distorted valves, calcified and changed as well as constricted, as the diagrams shown this morning have brought out. We have felt, for the reasons Dr. Harken has given, that the posterior cusp would be a good site for surgical attack; the anterior one has other functions to fulfill in directing blood to the aortic outlet. We have chosen the posterior cusp, but have been impressed by the fact that it is seldom more than one-half the total area of the anterior cusp, and is often less than that in the pathologic material studied in several centers, particularly in these mitral stenotic cases we are talking about. We have sought some means of dividing that calcified cusp, the margin not being divisible by any ordinary cutting edge; it is so resistant in many cases. We have sought a means of dividing that edge, preferably right back into the posterior cusp toward the base, to relieve the pulmonary and left auricular hypertension, to increase the ventricular inflow of blood during diastole, and we hoped that constriction of the base of the ventricle during systole would help to limit regurgitation. We have sought to do this without any loss of valve substance. That is the aim and the principle desired.

A method which we have not yet worked out as fully as we should like, but which may deserve further study, and we feel it does, came to mind from some basic work long ago by Sosman and Christian, who demonstrated quite a marked vertical motion of the heart fluoroscopically in cases where the calcified mitral valve could be observed. My colleague, Dr. Wilcox, demonstrated the same in a patient with a calcified annulus fibrosis, a marked vertical movement of the mitral ring and valve. To be sure this is not as great in extent as in the calcified aortic valve, but it is considerable.

The idea struck us that this motion might be used to advantage if one could pass a cutting type of instrument, such as a section of Gigli saw, down from above, through the left auricular appendage, or one of the pulmonary veins, and out through the apex of the heart. (Slide.) Both ends of the Gigli saw blade had been smoothed off in advance, or they may be encased in close-fitting segments of ureteral catheter. The middle section alone remains as a saw edge and this is maintained in close contact with the margin of the valve cusp to be sectioned by means of a combination of lengthwise traction on the ends of the saw, maintaining tension, and pressure exerted from the outside of the heart at the auriculoventricular ring. The principle is to maintain pressure of the valve cusp against the tense sawing edge, letting the cardiac motion do the actual sectioning of the valve. This technique causes very little blood loss and it does not disturb the cardiac action to any extent provided that the organ is not displaced greatly.

So far this method has not had adequate trial in human cases. We have had opportunity to use it only once. In retrospect, that patient was not truly suitable and little was gained. It is felt that this is simply a reflection of the difficulty in selecting really suitable cases. There is great need of a procedure which will enable us to tell preoperatively the size and condition of the cusps of the mitral valve and the state of the whole mitral ring.

Finally, it is suggested that during actual manipulation of rheumatic hearts, momentary compression of both carotid arteries in the neck by the anesthetist or an assistant may present cerebral embolic complications by fragments of valve or blood clot.

DR. O. C. BRANTIGAN, Baltimore.—All those who have contributed to this problem in the past certainly deserve great credit and surely the extensive experimental work has made possible the thoughts Dr. Bailey has upon this subject. I believe one should realize that he has made one very definite contribution, that is, the restoration of a functioning valve, this being obtained by dividing in the normal commissure and, particularly, in the commissure that is in the posterolateral direction so that the anterior leaf is in no way divided or injured. He has done away with the idea of a tunnel because the mechanical rigid tunnel makes hemorrhage control very difficult. By insertion of a finger through an opening of proper size in the auricular appendage very little blood is lost; if the opening is made too large a previously placed purse-string suture can be tightened enough to prevent bleeding. The finding of a normal commissure is done by digital palpation and not by guess, and if one will examine gross autopsy specimens or cadavers one will find this normal commissure is in a pretty definite location; it is difficult to find a true edge of the valve leaf but one can find between the chordae tendineae and papillary muscles a definite location for the commissure. In my experience in examining autopsy specimens and cadavers it is in a pretty definite location. With the cadaver in the usual operating position and the right index finger inserted into the auricular appendage the posterolateral commissure will be at about the medial aspect of the terminal phalanx of the finger. In the stenosed valve the finger, of course, will not pass through the opening, but the commissure location will be fairly definite.

I have recently had the pleasure of watching Dr. Bailey do one of his operations, the entire time consumed being very short, and the blood loss actually not more than two ounces. Following operation there was no murmur to be heard.

DR. DWIGHT E. HARKEN, Boston.—I was interested in Dr. Bailey's optimistic impression of our prospective 5 per cent mortality. I think that is a bit optimistic for 1949 but I believe that we can think of the reverse picture; namely, that there is a malignant disease under discussion. This malignant form of mitral stenosis is being more clearly defined. As we become better acquainted with mitral stenosis, we recognize a picture of hemoptysis, right ventricular failure, and gravely elevated intrapulmonic pressure (by catheterization) that gives us the picture of a malignant disease. It is perhaps more than an interesting coincidence that the only two patients who rejected surgery did die within three months after this refusal.

How to find the mitral orifice has been a problem that has bothered Dr. Bailey as much as it has bothered me. I believe the tunnel helps us. It is flexible and not associated with much clotting. I do not agree with Dr. Brantigan that the mitral ring is in a

constant position. It is not constant because there may or may not have been a prior period of regurgitation with ventricular hypertrophy. There may be varying degrees of pulmonic arterial dilatation and therefore the position of the mitral ring and also the position of the whole left auricle may vary greatly. The position and size of the appendage and also the mitral ring vary so much that in some instances it cannot be approached anterior to the phrenic nerve when the pericardium is opened. Even the appendage may lie posteriorly and require pericardial incision back of the phrenic nerve. These variations must be borne in mind.

Dr. Sweet's comments are timely. His results are extremely good. I hope that we can in time differentiate between patients who should have valvuloplasty and those who should have left to right shunts created.

I did not mean to imply today nor in previous publications in 1948 that I have wanted or accepted regurgitation. Even last year's publications repeatedly used the term "valvuloplasty" and "excision of the commissural zone and ring." A reprint of that paper was sent to Dr. Bailey at that time. One needs only to understand the function of the mitral valve by direct palpation in the laboratory animal to advocate valvuloplasty. As the finger is directed through the mitral ring of the animal, one discovers that the small posterior leaflet has little function and the area is closed by the ventricular systole, whereas the anterior leaflet in systole constitutes a wall that deflects or watersheds blood out through the aorta. Dr. Grace has very nicely emphasized this same point. As Dr. Grace also pointed out, and I thought my diagrams confirmed, the fishmouth opening in the funnel is quite eccentric; it is well back of the midpoint. I believe that point was not brought out in Dr. Bailey's report. These funnels are eccentric, the watershed is anterior, and the commissures are posterolateral and posteromedial. The mouth itself is rigid, the commissures are solidly closed, and the leaflets themselves are very flexible in the vast majority of instances. This concept of the pathologic process is fundamental.

In closing, I would again like to point out the fact that we are dealing with a malignant disease, the recognition of which may become clearer in time. Patients are not only to survive operations but be improved thereby. I hope that our surgical mortality becomes less formidable before we have another meeting.

DR. BAILEY.—It is evident from Dr. Sweet's report that life can be comfortably prolonged in many very seriously ill patients by the shunt operation which he has described, and I believe such an operation will always have a definite place in the surgical armory for the relief of mitral stenosis. However, it seems to me that it is not as good a procedure as one directed at the mitral valve itself, and when such direct surgery is perfected, shunt operations will find a very limited field of usefulness.

Dr. Harken and I may differ in terminology. It was my impression that he believed that a limited regurgitation or directed regurgitation was necessary for the relief of mitral stenosis. He performed a commissurotomy in his patients with a punch, which I believe was not large enough to cut all the way through the scar tissue and therefore did not produce a restoration of valve function. His method as described, however, is certainly a great improvement over the older procedures which produced free regurgitation.

I would like to point out that it is very easy to explore the valve and its commissures with the finger inserted through the auricular appendage. Because of the excessive left auricular pressure resulting from the mitral stenosis, the left auricular appendage and auricle are large and lend themselves to very adequate exploration with the finger. By the use of a purse-string suture about the base of the appendage, bleeding can be very readily controlled and is not serious. The purse-string is tied around the finger while it is in place within the appendage, so that no blood escapes during this part of the procedure.

Dr. Grace has pointed out that some of these valves are very calcified. We believe that in such cases if it is not possible to cut the commissures with the knife, it is possible to relieve the obstruction with a punch. For this purpose we have devised a narrow long-bladed backward-cutting forceps or punch which actually accomplishes the effect of commissurotomy even though it removes a small sliver of valvular tissue at the commissures.

At the present time we have formulated certain contraindications and indications for this procedure. We believe that active rheumatic infection, the presence of frank decompensation, and multivalvular lesions are contraindications. If the left ventricle is enlarged, one can be fairly certain that there is some other associated lesion and not pure mitral stenosis alone. Such lesions may include marked mitral regurgitation or aortic stenosis and regurgitation. The presence of subacute bacterial endocarditis and lesions in patients over the age of 40 years are further contraindications. We feel that the ideal indication for commissurotomy is (pure) mitral stenosis with no, or very early, symptoms, provided the pressure in the right ventricle and pulmonary artery can be demonstrated to be elevated. If pulmonary hypertension has begun to develop, these patients will undoubtedly run into serious cardiac difficulties within two to three years. If they are operated upon before serious symptoms have developed, not only can the valve be surgically treated more effectively, but the ultimate result will also be much improved. If a patient has had a previous bout of cardiac decompensation but can be satisfactorily restored to compensation by medical means, such a patient may still be subjected to surgery and a good result obtained. After further experience it is possible that future indications might include cases complicated by other valvular lesions, and possibly even those who are in mild decompensation, no further improvement under medical management being obtainable.

ACIDOSIS DURING THORACIC SURGERY

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THE chain of events that leads to success or failure in thoracic surgery is more complex than it is in other fields. Notwithstanding the progress made in recent years, the occasional patient succumbs near the end of operation or shortly thereafter, or more often barely pulls out of a puzzling condition of low blood pressure. At such times it is customary to say, "The blood replacement was not sufficient," or, "His heart just would not stand it," and so on. Stand what is often not clear.

The purpose of this paper is to present factual data that explain some of the unsatisfactory experiences mentioned. We shall describe an acidosis of potentially fatal degree that results from accepted procedures in thoracic surgery, an acidosis that increases smoothly and swiftly with the passage of time.

POSITION OF PATIENTS AND ANESTHESIA PROCEDURES

Our anesthesia procedures have been described in detail elsewhere.[2, 3] Briefly, our patients are operated upon with the diseased side vertically uppermost with a blanket roll or pillow of approximately five inches in diameter placed beneath the thorax. About 5 degrees of Trendelenburg position is used, and then the operating table is broken 10 to 15 degrees at the head and 5 degrees at the foot.

Preanesthetic medication consists in most cases of morphine, 10 mg., and atropine, 0.6 mg., subcutaneously. Unconsciousness is induced with 80 volumes per cent nitrous oxide with 20 volumes per cent oxygen, and then the shift is made to straight ether maintenance with 95 volumes per cent oxygen in a closed system, usually with "circle" soda lime filter. Endotracheal tubes are always used, Flagg, size 8, or Magill, 32 French. Inflatable cuffs are not used on the endotracheal tubes employed in these cases. (We do sometimes use them in transthoracic esophagectomy where the positive pressure needed can cause troublesome gastric distention.) Positive pressure is used when necessary to provide normal oxygenation of the blood, to reduce mediastinal swing, and to inflate the lungs at about twenty-minute intervals. Aspiration of the bronchi is carried out to maintain a clear airway.

CHEMICAL METHODS

Samples.—Blood was drawn from the radial artery in oiled syringes and transferred under oil. Heparin was used to prevent coagulation in that part of the blood used for the oxygen determination. Carbon dioxide and pH were measured in serum. The first blood sample was drawn immediately before the induction of anesthesia while the patient breathed room air, and subsequent samples were drawn while the patient was connected with the closed anesthesia apparatus.

From the Anesthesia Laboratory of the Harvard Medical School at the Massachusetts General Hospital.

Read at the Twenty-ninth Annual Meeting of The American Association for Thoracic Surgery, New Orleans, La., March 29-31, 1949.

Oxygen.—Oxygen was determined by the method of Van Slyke and Neill.[15] When the blood contained ether, the Snyder[14] modification of the Shaw and Downing[13] method was used. In this procedure the oxygen and carbon dioxide, after extraction from the blood, are stored in a pipette attached to the machine while the vacuum chamber is cleaned. Water is substituted for the ferricyanide, the gases returned to the chamber, and the analysis continued as in the original method. One cubic centimeter samples were used. Oxygen capacities were determined on all samples by aerating the blood in room air for about five minutes.

Carbon Dioxide.—Carbon dioxide determinations were made on 0.5 c.c. serum by the Van Slyke and Neill method.[15] When ether was present in the blood, the Austin[1] method was used with some modification, as follows: The serum is acidified and extracted in the usual manner except that one very small drop of caprylic alcohol is used instead of the usual two drops. The p_1 is read, the extraction is repeated, and p_1 is read again. The mercury is allowed to rise in the chamber to the 2 c.c. mark at the same rate as in an analysis without ether. The carbon dioxide is absorbed with 0.25 c.c. of 5 N NaOH, and p_2 is read. The mercury is lowered to the 50 c.c. mark, and the chamber is shaken for three minutes. The volume is reduced to 2 c.c., and p_3 is read. This is repeated until p_3 is constant. If there is sufficient caprylic alcohol to prevent foaming but not enough to form a layer above the solution in the vacuum chamber, then p_1 and p_2 readings will check themselves within 0.5 mm. The volume of the acidified solution extracted was 3.5 c.c. when 0.5 c.c. of serum was used. The K for the machines under these conditions was 0.64. The formula used $[CO_2] = [p_1 - p_3 + K\ (p_3 - p_2)] \times f$.

Carbon Dioxide Tension.—The carbon dioxide tension was calculated from the carbon dioxide content (volumes per cent) and the pH value. In most cases this was read off the Peters and Van Slyke chart.[10] When the values were beyond the limits of this, the Henderson-Hasselbalch equation was used directly to calculate the tension,

$$p = \frac{CO_2}{0.1316 \times 0.510\ (10^{pH - pK^1 + 1})}.$$

When the pH is in the neighborhood of 7.0 it is not possible to estimate the carbon dioxide tension with as great accuracy as when the pH is higher, since small changes in pH in the low region cause relatively large changes in the carbon dioxide tension.

Hydrogen-ion Concentration.—Hastings and Sendroy[9] phenol red bicolor standards for studies in acidosis were used for the pH: 0.2 c.c. of serum were added to 4.0 c.c. of saline phenol red solution previously adjusted to 7.45. Then 0.2 c.c. serum in 4.0 c.c. saline solution was used as a blank. These were warmed to 38° C., placed in the colorimeter block, and matched to the nearest set of standards. The standards can be read for every 0.05 change in the pH and the final reading on the serum can be estimated to 0.02 pH.

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Hematocrit Value.—Hematocrit value was determined on heparinized blood in Rourke-Ernstene[12] tubes which were spun at 2,500 r.p.m. for forty-five minutes.

RESULTS

The principal data obtained in 43 patients, in two age groups, are given in Tables I to VI. They are summarized in Table VII, A in order to compare the patient's state near the end of operation with what it was at the beginning. The average data in Table VII, A show that while the carbon dioxide content remained constant, the pH decreased sharply in the lobectomy and pneumonectomy groups. These findings in corrected form, in conjunction with the calculated increases in fixed acid shown in Table VII, B, indicated that these patients were in a rather severe acidosis of combined respiratory and metabolic types.

Table VIII shows that the rise in alveolar carbon dioxide tension began and developed to a significant degree before the pleura was opened. And finally, Table IX demonstrates that the anesthetic agent or apparatus was not responsible for the rise in carbon dioxide tension. Table X illustrates how assisted respiration was effective in lowering the carbon dioxide tension in one case but not in another.

Attention is called to the fact that the oxygen tensions shown in these tables are generally satisfactory, even near the termination of pneumonectomy, and at a time when the carbon dioxide tensions are dangerously high.

There is some suggestion in the pneumonectomy group that the hematocrit rises during operation, but an examination of the standard errors of the means does not indicate significance in the available data.

DISCUSSION

In the normal, unanesthetized man an increase in the concentration of carbon dioxide in the inspired air results in an increase in pulmonary ventilation, until about 9 per cent is reached. Further increase in carbon dioxide causes depression of the respiration,[11] presumably owing to the well-known anesthetic properties of the gas.

Under our present circumstances no such respiratory response to the high tensions of carbon dioxide was evident, probably because of the depressing action of ether on the respiratory center.[6]

It is quite clear from Fig. 1 that under present circumstances (unlike the normal), respiration which is adequate to provide oxygen is not adequate to remove carbon dioxide. Preoccupation with color of a patient's blood, important as this is, is not enough. This is only half of the problem. The carbon dioxide level must also be considered. The tensions of this gas reached in some of our patients might of themselves be fatal, particularly in patients who had been subjected to considerable blood loss and surgical trauma.

Why the carbon dioxide tension should rise so high must be considered. This is not the usual effect of ether with patients in the supine position (see Table IX). Presumably this great rise is to be blamed on position and the open

pleura and the depression of respiration by the anesthetic. Some facts to be examined in this connection are the following.

In eleven patients (Table VIII) the alveolar carbon dioxide tension was determined immediately prior to the induction of anesthesia and then some forty-two minutes later, but before the pleura was opened. (These patients had been in the operative position with the diseased side uppermost for approximately twenty minutes of this time.) Ten of these eleven patients showed a rise of 14.6 mm. Hg or 2.0 volume per cent, average. Thus, the alveolar carbon dioxide tension had begun to swing up sharply before the pleura was opened and while the tidal volume and minute volume of respiration appeared to be quite normal. The open pleura is therefore not the only factor responsible for the later rise in carbon dioxide tension.

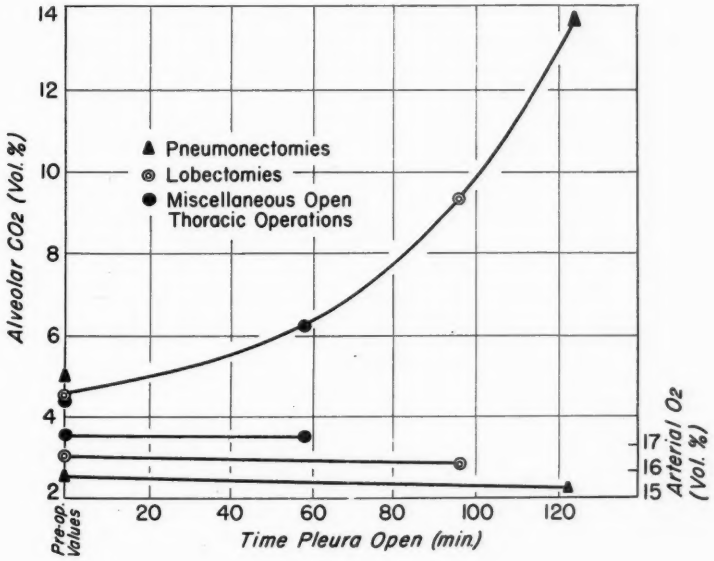

Fig. 1.

It must be emphasized that this increase in alveolar tension of 14.6 mm. Hg., or 2.0 volume per cent, is a truly great rise. It has been found (Campbell, Douglas, Haldane, and Hobson[5]) in the average individual that a rise in pressure of 1.6 mm. Hg will double pulmonary ventilation. In the normal unanesthetized man a rise of only 1.0 volume per cent in the alveolar carbon dioxide content is sufficient to increase the pulmonary ventilation about 50 liters per minute.

How can this early rise in alveolar tension of carbon dioxide be explained? A number of factors are present: besides the position, we must consider the increase in dead space produced by the anesthesia apparatus, the effect of the endotracheal tube, and possibly the effect of the anesthetic agent on the bronchiolar musculature. Conceivably an increase in dead space could be caused by the

TABLE I. PNEUMONECTOMIES

PATIENT	AGE (YR.)	DURATION OF ANESTHESIA (MIN.)	PLEURA	TIME AFTER ANESTHESIA STARTED (MIN.)	TIME AFTER PLEURA OPENED (MIN.)	O_2 CONTENT (VOL. %)	O_2 CAPACITY (VOL. %)	% SATURATION	CO_2 CONTENT (VOL. %)	pH	ALVEOLAR CO_2 TENSION	HEMATOCRIT % CELLS	REMARKS
B. W.	49	190	Adherent	0	0	12.6	12.8	99	56.8	7.44	37.4	34.2	March 25
				30	0	14.0	12.5	89	55.5	7.40	39.5	36.9	March 25
				75	25	15.3	13.9	91	62.5	7.27	59.5	39.0	March 25
				168	118	14.0	14.3	98	62.3	7.07	90.0	42.8	March 25
C. B.	57	260	Adherent	0	0	17.2	17.4	99	52.0	7.55	26.3	45	Feb. 16
				230	180	15.7	17.4	90	72.3	7.03	115.8	46	Feb. 16
				246	196	17.3	17.4	99	68.5	7.08	96.7	46	Feb. 16
						18.7	18.9	99	56.5	7.45	36.0	44	Feb. 17
W. J.	54	200	Adherent	0	0	12.4	13.5	91.7	56.5	7.50	33.3	34.5	Feb. 12
				30	0	14.2	13.4	100	65.3	7.15	84.0	37.3	Feb. 13
				90	50	13.2	13.5	97.7	61.8	7.15	82.5	37.8	Feb. 13
				175	135	15.5	15.5	100	71.4	7.08	100.6	43.2	Feb. 13
						14.1	16.3	86.5	64.6	7.40	48.0	42.6	Feb. 17
H. V.	41	170	Adherent	0	0	17.1	17.5	97.7	55.7	7.45	36.5	39.7	March 13
				40	0	18.8	19.1	98.5	57.6	7.28	53.0	44.4	March 13
				128	83	18.5	19.3	95.7	58.3	7.25	60.0	42.8	March 13
				175	130	17.8	18.0	98.8	52.5	7.28	50.2	44.6	March 13
						14.1	14.7	95.7	60.2	7.57	30.3	35.2	March 18
L. T.	18	120	Adherent	0	0	15.2	16.4	92.7	63.9	7.55	32.5	41.1	Dec. 18
				38	0	15.9	16.3	97.5	61.5	7.35	49.0	46.6	Dec. 19
				85	40	14.1	15.5	91.0	67.5	7.15	84.0	46.6	Dec. 19
				130	85	10.3	14.1	73.2*	70.9	7.00	133.1	44.7	Dec. 19
						17.2	17.1	100	66.0	7.50	37.5	43.8	Dec. 24
						16.2	16.8	97	63.2	7.57	30.7	44.0	Dec. 27
						17.4	17.9	97.2	59.7	7.50	33.9	43.8	Feb. 17
C. B.	36	190	Adherent	0	0	18.0	18.5	97.3	62.4	7.45	39.5	43.7	Sept. 20
				0	0	18.0	18.5	97.2	61.4	7.45	39.0	43.1	Sept. 22
				60	15	18.7	19.8	95	69.8	7.18	79.5	52.2	Sept. 22
						16.3	17.0	96	59.5	7.45	38.0	44.3	Sept. 22
						13.2	14.5	91	57.4	7.48	33.8	36.9	Sept. 23
									59.0	7.55	30.0		Sept. 30
E. L.	24	230	Free	0	0	17.1	18.5	92.5	60.6	7.46	37.3	45.8	May 15
				40	0	20.8	20.6	100	59.4			52.2	May 16
				93	37	18.1	19.8	91.5	55.3			58.4	May 16
				200	144	17.2	18.4	93.5	58.2			54.0	May 16
						18.5	18.6	100	56.7			50.0	May 17
R. H.	13	170	Adherent	0	0	12.6	14.5	86.9		7.48	34.5	43.4	May 22

				200	144	17.2 18.5	18.4 18.6	93.5 100	58.2 56.7			54.0 50.0	May 16 May 17
B. H.	13	170	Adherent	0	0	12.6	14.5	86.9		7.48	34.5	43.4	May 22
				40	0	18.1	17.7	100				50.0	May 23
				120	77	17.8	17.3	100				45.0	May 23
				155	112	16.9	16.7	100				48.6	May 23
						17.9	17.5	100		7.37		53.3	May 26
M. F.	34	170	Adherent	0	0	13.3	14.7	90.5	59.8	7.45	37.8	37.5	July 2
				72	0	14.2	15.3	93	59.7			41.2	July 2
				117	35	14.4	14.5	100	56.8			38.7	July 2
				157	75	14.6	15.2	96	53.2			40.4	July 2
L. M.	19	220	Adherent	45	0	19.5			52.7			48.3	July 26
				105	40	19.6			62.6			47.9	July 26
				220	155	17.7			50.5			45.2	July 26
P. F.	49	240	Adherent	36	0	17.0			63.0			47.1	July 29
				92	46	16.4			66.5			47.9	July 29
				144	98	15.2			68.9			45.9	July 29
				182	136	15.6			67.2			46.1	July 29
				217	171	16.4			61.3			47.8	July 29
R. D'E.	34	190	Adherent	27	0							45.0	April 3
				40	0	16.8			42.3			45.8	April 3
				65	14	13.5			46.1			47.0	April 3
				108	57	12.4			49.6			48.4	April 3
				190	139	13.8			50.3			54.7	April 3
T. F.	28	170	Adherent	65	0	16.6			58.2			41.0	April 17
				110	37	16.1			58.0			41.4	April 17
				160	87	12.9			54.7				April 17
				178	105	13.0			50.3			40.9	April 17
J. D.	52	230	Adherent	35	0	21.1			68.2			49.5	July 10
				95	42	20.1			64.3			47.9	July 10
				146	93	19.5			65.7			49.6	July 10
				193	140	17.7			60.6			46.4	July 10
				230	177				57.1			47.6	July 10
W. N.	23	260	Adherent	67	0				58.4				Dec. 22
				97	25	18.7			58.3				Dec. 22
				142	70	16.3			60.3				Dec. 22
C. H.	60	180	Free	49	0	10.1			73.8			Exceed-	Feb. 15
				63	4	13.0			75.3			ingly	Feb. 15
				115	56	12.1			72.8			high,	Feb. 15
				150-161	91-102				74.8			above 70%	Feb. 15

*Floods of pus in airway.

TABLE II. LOBECTOMIES

PATIENT	AGE (YR.)	DURATION (MIN.)	PLASMA	TIME AFTER ANESTHESIA STARTED (MIN.)	TIME AFTER PLEURA OPENED (MIN.)	O_2 CONTENT (VOL. %)	O_2 CAPACITY (VOL. %)	% SATURATION	CO_2 CONTENT (VOL. %)	pH	ALVEOLAR CO_2 TENSION	HEMATOCRIT % CELLS	REMARKS
H. C.	23	170	Adherent	0	0	14.9	15.3	97.3	59.8	7.50	34.0	38.2	Dec. 20
				40	0	15.6	15.9	98.0	65.2	7.35	51.0	39.3	Dec. 22
				100	45	15.8	15.3	100	67.6	7.27	63.0	38.8	Dec. 22
				175	120	15.6	15.7	100	68.3	7.23	69.0	41.7	Dec. 22
						13.5	14.4	93.7	64.9	7.45	41.0	36.6	Dec. 23
M. N.	59	70	Adherent	0	0	14.6	15.5	94.2	57.4	7.48	33.8	39.8	Oct. 8
				0	0	15.0	15.5	96.7	59.7	7.55	30.3	37.8	Oct. 9
				40	0	17.7	17.3	100	51.0	7.55	26.1	43.3	Oct. 9
				93	48	12.5	15.3	81.7	63.6	7.25	61.0	40.8	Oct. 9
G. B.	46	190		0	0	13.4	14.3	94	60.1			39.7	June 4
				48	0	14.5	14.8	98	56.3			43.0	June 4
				102	48	13.6	14.4	95	64.5			42.2	June 4
				183	129		14.7		60.9			43.8	June 4
E. M.	27	190		0	0	14.6	16.0	91.4	60.6			38.8	April 21
				33	0	16.3	15.7	100	55.7			40.2	April 21
				159	119	14.9	14.2	100	47.4			42.0	April 21
						12.2	13.0	94	61.6			34.1	April 22
						11.6	12.1	95.8	64.3			32.2	April 23
						13.0	14.8	87.8	58.4			37.3	May 7
E. C.	12	170	Adherent	45	0	18.1	17.6	100	71.4			47.1	May 8
				95	40	16.6	17.6		69.5			48.5	May 8
				135	80	15.5	15.1	100	61.6			48.5	May 8
D. E.	23	130		41	0	18.9			56.2			41.6	April 18
				76	27	18.5			55.4			42.5	April 18
				132	83	17.3			49.5			40.0	April 18
A. I.	18	230	Adherent	45	0	23.8			61.5			55.3	July 8
				100	38	23.8			56.8			55.5	July 8
				150	88	22.6			56.9			56.0	July 8
				205	143	19.2			59.7			52.5	July 8
				235	173				55.4			57.5	July 8
A. A.	40	150	Adherent	0	0	15.4	16.3	94.5	60.7	7.50	35.8	39.9	March 16
				40	0	16.8	16.7	100	52.5	7.40	38.2	41.5	March 16
				85	35	16.4	17.0	96.5	56.0	7.30	51.7	39.5	March 16
				170	120	15.8	16.3	97.0	55.7	7.30	51.5	36.0	March 16
						13.8	14.0	100	52.5	7.48	32.0	38.8	March 17
K.K.	54	160	Free	0	0	16.4	16.5	100	61.4	7.55	31.5	41.7	Oct. 8
				38	0	19.3	17.9	100	60.8	7.37	46.5	42.9	Oct. 8

					15.8	14.0	100	52.5	7.48	32.0	38.8	March 17
K.K.	54	160	Free	0	0	16.4	16.5	100	61.4	7.55	31.5	41.7	Oct. 8
				38	0	19.3	17.9	100	60.8	7.37	46.5	42.9	Oct. 8
				86	24	19.1	17.7	100	69.6	7.22	72.5	45.6	Oct. 8
				132	70	19.1	17.6	100	65.9	7.18	76.0	47.1	Oct. 8
F.S.	55	255	Adherent	0	0	17.9	18.3	97.9	59.7	7.55	31.5	48.0	Oct. 28
				35	0	20.7	19.0	100	69.0	7.30	60.5	52.3	Oct. 28
				130	68	19.1	18.7	100	68.6	7.10	88.0	52.5	Oct. 28
				228	166	18.1	18.8	96.3	68.1	7.05	103.0	51.1	Oct. 28
R. M.	31	190	Adherent	0	0	18.0	18.9	95.3	48.8	7.50	27.8	44.4	Dec. 31
				40		17.8	17.5	98.5	48.0	7.45	30.0	45.0	Dec. 31
				105		16.6	16.8	98.7	53.5	7.20	62.0	44.3	Dec. 31
				190		16.3			49.9	7.10	68.0	45.3	Dec. 31
R. R.	55	150	Free	0	0	14.7	15.6	94.2	55.7	7.47	34.7	37.2	Feb. 9
				44	0	17.7	17.8	100	59.2	7.28	54.0	44.8	Feb. 9
				91	44	17.2	16.8	100	59.8	7.28	56.0	44.5	Feb. 9
				132	85	17.8	16.7	100	62.3	7.28	58.0	45.6	Feb. 9
K.P.	34	240	Adherent	0	0	16.3	17.6	93	65.2	7.53	34.4	43.4	Nov. 12
				55	0	18.4	17.5	100	60.0	7.45	37.8	45.2	Nov. 13
				110	45	19.1	18.4	100	63.6	7.38	46.5	46.7	Nov. 13
				180	115	18.7	17.7	100	60.7	7.37	46.0	48.9	Nov. 13
						15.9	15.8	100	62.3	7.47	38.0	43.6	Nov. 14
						18.7	19.6	95	62.3	7.55	32.0	48.4	Jan. 6
Y. B.	30	120	Adherent			16.8			56.3				Oct. 9
						13.9			63.5				Oct. 9
J. P.	28	210	Adherent	45	0	18.0			51.3			43.6	July 19
				96	46	18.9			53.7			43.5	July 19
				184	134	18.6			47.9			44.1	July 19
				225	175				40.7			48.0	July 19
E. K.	37	145	Adherent	40	0	17.2			56.4				Oct. 6
				93	48	14.5			67.9				Oct. 6
				119	74	14.4			57.5				Oct. 6
E. B.	47	170	Free	50	0	15.3			57.6				Oct. 13
				90	30	15.2			59.2				Oct. 13
				120	60	14.6			60.0				Oct. 13
				150	90	14.8			56.0				Oct. 13
P. S.	15	160	Free	47	0	13.8			43.0				Oct. 25
				122	67	14.6			49.0				Oct. 25
V. B.	16	240	Adherent	50	0	16.8			52.9				Nov. 16
				155	95				51.1				Nov. 16
F. DiP.	27	150	Adherent	62	0				53.8				Feb. 16
				66	0	18.3			51.9				Feb. 16
				105	30	18.1			56.2				Feb. 16

TABLE III. MISCELLANEOUS

PATIENT	AGE (YR.)	OPERATION	DURATION OF ANESTHESIA (MIN.)	PLEURA	TIME AFTER ANESTHESIA STARTED (MIN.)	TIME AFTER PLEURA OPENED (MIN.)	O_2 CONTENT (VOL. %)	O_2 CAPACITY (VOL. %)	% SATURATION	CO_2 CONTENT (VOL. %)	pH	ALVEOLAR CO_2 TENSION	HEMATOCRIT % CELLS	REMARKS
E. A.	64	Inoperable cancer	115	Free	0	0	15.2	15.9	96	57.4	7.48	34.0	38	Feb. 11
					90	40	15.7	16.0	98	56.4	7.43	37.0	39	Feb. 11
E. D.	52	Excision of cyst of mediastinum	130	Adherent	0	0	17.0	17.8	95.5	59.2	7.55	30.5	43.3	Dec. 29
					55	0	18.4	18.3	100	57.9	7.45	36.6	43.7	Dec. 29
					135	70	17.3	16.9	97.6	56.4	7.45	36.3	40.4	Dec. 29
G. C.	31	Enucleation of tumor	160	Free	0	0	18.4	18.6	98.9	60.1	7.53	31.9	47.4	Oct. 15
					50	0	17.4	17.5	99	51.3	7.55	26.3	48.3	Oct. 17
					115	55				55.2	7.42	37.8	47.8	Oct. 17
E. L.	60	Inoperable exploratory thoracotomy	55		0	0	15.0	16.7	89.7	57.8	7.55	28.8	44.1	Oct. 15
					38	0	17.0	17.7	100	61.9	7.30	54.0	48.0	Oct. 16
					57	12	16.9	16.8	100	61.3	7.26	58.1	48.0	Oct. 16
H. L.	42	Excision of cyst of mediastinum	180	Free	41	0	23.1			57.3			53.6	Apr. 22
					88	38	20.6			59.1			52.0	Apr. 22
					145	95	21.8			58.7			51.5	Apr. 22
R. T.	55	Inoperable carcinoma of right lower lobe	80	Free	27	0	17.1			55.5			43.1	March 25
					42	10	16.0			60.4			44.5	March 25
					55	23	15.0			56.5			43.7	March 25
W. B.	27	Segment left lower lobectomy and lingulectomy	160	Adherent	0	0	17.8	18.9	94.3	59.2	7.47	36.0	45.8	Sept. 24
					35	0	18 6	20.9	100	57.4	7.32	49.0	47.0	Sept. 24
					88	45	17.0	18.8	90.4	56.9	7.34	47.0	50.6	Sept. 24
					150	107	18.6	20.0	93.0	57.3	7.30	50.5	51.2	Sept. 24
							20.6	19.4	100	56.0	7.43	37.0	44.2	Sept. 24
							19.0	19.1	100	61.1	7.43	40.0	50.0	Sept. 25

TABLE IV, A. PNEUMONECTOMIES

PATIENT	SEX	AGE (YR.)	BLOOD BEFORE OPERATION			BLOOD AT END OF OPERATION			BLOOD DAY FOLLOWING OPERATION		
			CO_2 CONTENT (VOL. %)	pH	ALVEOLAR TENSION CO_2 (MM.HG)	CO_2 CONTENT (VOL. %)	pH	ALVEOLAR TENSION CO_2 (MM.HG)	CO_2 CONTENT (VOL. %)	pH	ALVEOLAR TENSION CO_2 (MM.HG)
44 Years and Under											
W. N.	♂	23	58.4			60.3					
R. d'E.	♂	34	42.3			50.3					
T. F.	♀	28	58.2			50.3					
L. M.	♀	19	52.7			50.5					
E. L.	♂	24	60.6	7.46	37.3	58.2			56.7		
B. H.	♂	13	58.2	7.48	34.5	59.7			57.8	7.37	43.0
M. F.	♀	34	59.8	7.45	37.8	53.2					
C. B.	♂	36	62.4	7.45	39.5				57.4	7.48	33.8
L. T.	♂	18	63.9	7.55	32.5	70.9	7.00	133.1	66.0	7.50	37.5
H. V.	♀	41	55.7	7.45	36.5	52.5	7.28	50.2	60.2	7.57	30.3
Average			57.2	7.47	36.4	56.2			59.6	7.48	36.2
45 Years and Over											
C. H.	♂	60	73.8			74.8					
J. D.	♂	52	68.2			57.1					
P. F.	♂	49	63.0			61.3					
W. J.	♂	54	56.4	7.50	33.3	71.4	7.08	100.6	64.6	7.40	48.0
B. W.	♂	49	56.8	7.44	37.4	62.3	7.07	90.0			
C. B.	♂	57	52.0	7.55	26.3	72.3	7.03	115.8	56.5	7.45	36.0
Average			61.7	7.50	32.3	66.5					
Grand average			58.9	7.48	35.0	60.3	7.09	97.9	59.9	7.46	38.1

TABLE IV, B. PNEUMONECTOMIES

PATIENT	SEX	AGE (YR.)	DURATION OF ANESTHESIA (MIN.)	BLOOD TAKEN BEFORE OPERATION				BLOOD TAKEN AT END OF OPERATION					BLOOD TAKEN DAY FOLLOWING OPERATION			
				O_2 CONTENT (VOL. %)	O_2 CAPACITY (VOL. %)	% SATURATION	HEMATOCRIT % CELLS	TIME AFTER PLEURA OPENED (MIN.)	O_2 CONTENT (VOL. %)	O_2 CAPACITY (VOL. %)	% SATURATION	HEMATOCRIT % CELLS	O_2 CONTENT (VOL. %)	O_2 CAPACITY (VOL. %)	% SATURATION	HEMATOCRIT % CELLS
44 Years and Under																
W. N.	♂	23	260					70	16.3							
R. d'E.	♂	34	190	16.8			45	139	13.8			55				
T. F.	♀	28	170	16.6			41	105	13.0			41				
L. M.	♀	19	220	19.5			48	155	17.7			45				
E. L.	♂	24	230	17.1	18.5	93	46	144	17.2	18.4	93	54	18 5	18.6	99	50
B. H.	♂	13	170	12.6	14.5	87	43	112	16.9	16.7	100+	49	17.9	17.5	100+	53
M. F.	♀	34	170	13.3	14.7	91	38	75	14.6	15.2	96	40				
C. B.	♂	36	190	18.0	18.5	98	44						13.2	14.5	91	37
L. T.	♂	18	120	15.2	16.4	93	41	40	10.3	14.1	73	45	17.2	17.1	100	44
H. V.	♀	41	170	17.1	17.5	98	40	130	17.8	18.0	99	45	14.1	14.7	96	35
Average				16.2	16.7	93	43	107	15.3	16.5	92	47	16.2	16.5	97	44
45 Years and Over																
C. H.	♂	60	180	10.1				97	12.1							
J.D.	♂	52	230	21.1			50	140	17.7			46				
P. F.	♂	49	240	17.0			47	171	16.4			48				
W. J.	♂	54	200	12.4	13.5	92	35	135	15.5	15.5	100	43	14.1	16.3	87	43
B. W.	♂	49	190	12.6	12.8	99	34	118	14.0	14.3	98	43				
C. B.	♂	57	260	17.2	17.4	99	45	180	15.7	17.4	90	46	18.7	18.9	99	44
Average				15.1	14.6	97	42	140	15.2	15.7	96	45				
Grand average				15.7	16.0	94	43	122	15.3	16.2	94	46	16.2	16.8	96	44

TABLE V, A. LOBECTOMIES

PATIENT	SEX	AGE (YR.)	BLOOD BEFORE OPERATION			BLOOD AT END OF OPERATION			BLOOD DAY FOLLOWING OPERATION		
			CO_2 CONTENT (VOL. %)	pH	ALVEOLAR TENSION CO_2 (MM.Hg)	CO_2 CONTENT (VOL. %)	pH	ALVEOLAR TENSION CO_2 (MM.Hg)	CO_2 CONTENT (VOL. %)	pH	ALVEOLAR TENSION CO_2 (MM.Hg)
44 Years and Under											
E. K.	♂	37	56.4			57.5					
Y. B.	♀	30	56.3			63.5					
P. S.	♂	15	43.0			49.0					
V. B.	♀	16	52.9			51.1					
F. diP.	♂	27	51.9			56.2					
D. E.	♀	23	56.2			49.5					
A. I.	♂	18	61.5			59.7					
J. P.	♀	28	51.3			47.9					
E. M.	♂	27	60.6			47.4			61.6		
E. C.	♀	12	71.4			61.6					
K. P.	♂	34	65.2	7.53	34.4	60.7	7.37	46.0	62.3	7.47	38.0
H. C.	♂	23	59.8	7.50	34.0	68.3	7.23	69.0	64.9	7.45	41.0
R. M.	♀	31	48.8	7.50	27.8	49.9	7.10	68.0			
A. A.	♂	40	60.7	7.50	35.8	55.7	7.30	51.5	52.5	7.48	32.0
Average			56.9	7.51	33.0	55.6	7.25	58.6	60.3	7.47	37.0
45 Years and Over											
E. B.	♀	47	57.6			56.0					
G. B.	♂	46	60.1			64.5					
M. N.	♂	59	57.4	7.48	33.8	63.6	7.25	61.0			
R. R.	♂	55	55.7	7.47	34.7	62.3	7.28	58.0			
K. K.	♂	54	61.4	7.55	31.5	65.9	7.18	76.0			
F. S.	♂	55	59.7	7.55	31.5	68.1	7.05	103.0			
Average			58.6	7.51	32.9	63.4	7.19	74.5			
Grand average			57.4	7.51	32.9	57.9	7.22	66.6	60.3	7.47	37.0

TABLE V, B. LOBECTOMIES

PATIENT	SEX	AGE (YR.)	DURATION OF ANESTHESIA (MIN.)	BLOOD TAKEN BEFORE OPERATION				BLOOD TAKEN AT END OF OPERATION					BLOOD TAKEN DAY FOLLOWING OPERATION			
				O_2 CONTENT (VOL. %)	O_2 CAPACITY (VOL. %)	% SATURATION	HEMATOCRIT % CELLS	TIME AFTER PLEURA OPENED (MIN.)	O_2 CONTENT (VOL. %)	O_2 CAPACITY (VOL. %)	% SATURATION	HEMATOCRIT % CELLS	O_2 CONTENT (VOL. %)	O_2 CAPACITY (VOL. %)	% SATURATION	HEMATOCRIT % CELLS
44 Years and Under																
E. K.	♂	37	145	17.2				74	14.4							
Y. B.	♀	30	120	16.8					13.9							
P. S.	♂	15	160	13.8				67	14.6							
V. B.	♀	16	240	16.8				95								
F. di'P.	♂	27	150	18.3				30	18.1							
D. E.	♀	23	130	18.9			42	83	17.3			40				
A. I.	♂	18	230	23.8			55	143	19.2			53				
J. P.	♀	28	210	18.0			44	134	18.6			44				
E. M.	♂	27	190	14.6	16.0	91	39	119	14.9	14.2	100+	42	12.2	13.0	94	34
E. C.	♀	12	170	18.1	17.6	100+	47	80	15.5	15.1	100+	49				
K. P.	♂	34	240	16.3	17.6	93	43	115	18.7	17.7	100+	49	15.9	15.8	100	44
H. C.	♂	23	170	14.9	15.3	97	38	120	15.6	15.7	99	42	13.5	14.4	94	37
R. M.	♀	31	190	18.0	18.9	95	44	130	16.3			45				
A. A.	♂	40	150	15.4	16.3	95	40	120	15.8	16.3	97	36	13.8	14.0	100	39
Average				17.2	17.0	95	44	101	16.4	15.8	99	44	13.9	14.3	97	38
45 Years and Over																
E. B.	♀	47	170	15.3				90	14.8							
G. B.	♂	46	190	13.4	14.3	94	40	48	13.6	14.4	95	42				
M. N.	♂	59	70	14.6	15.5	94	40	48	12.5	15.3	82	41				
R. R.	♂	55	150	14.7	15.6	94	37	85	17.8	16.7	100+	46				
K. K.	♂	54	160	16.4	16.5	99	42	70	19.1	17.6	100+	47				
F. S.	♂	55	255	17.9	18.3	98	48	166	18.1	18.8	96	51				
Average				15.4	16.0	96	41	85	16.0	16.6	95	45				
Grand average				16.7	16.5	95	43	96	16.2	16.2	97	45	13.9	14.3	97	38

TABLE VI, A. MISCELLANEOUS

PATIENT	SEX	AGE (YR.)	BLOOD BEFORE OPERATION			BLOOD AT END OF OPERATION			BLOOD DAY FOLLOWING OPERATION		
			CO_2 CONTENT (VOL. %)	pH	ALVEOLAR TENSION CO_2 (MM.Hg)	CO_2 CONTENT (VOL. %)	pH	ALVEOLAR TENSION CO_2 (MM.Hg)	CO_2 CONTENT (VOL. %)	pH	ALVEOLAR TENSION CO_2 (MM.Hg)
44 Years and Under											
H. L.	♂	42	57.3			58.7					
W. B.	♂	27	59.2	7.47	36.0	57.3	7.30	50.5	61.1	7.43	40.0
G. C.	♂	31	60.1	7.53	31.9	55.2	7.42	37.8			
45 Years and Over											
R. T.	♂	55	55.5			56.5					
E. L.	♀	60	57.8	7.55	28.8	61.3	7.26	58.1			
E. D.	♀	52	59.2	7.55	30.5	56.4	7.45	36.3			
E. A.	♂	64	57.4	7.48	34.0	56.4	7.43	37.0			
Average			58.1	7.52	32.2	57.4	7.37	43.9			

TABLE VI, B. MISCELLANEOUS

PATIENT	SEX	AGE (YR.)	DURATION OF ANESTHESIA (MIN.)	BLOOD TAKEN BEFORE OPERATION				BLOOD TAKEN AT END OF OPERATION					BLOOD TAKEN DAY FOLLOWING OPERATION				OPERATION
				O_2 CONTENT (VOL. %)	O_2 CAPACITY (VOL. %)	% SATURATION	HEMATOCRIT % CELLS	TIME AFTER PLEURA OPENED (MIN.)	O_2 CONTENT (VOL. %)	O_2 CAPACITY (VOL. %)	% SATURATION	HEMATOCRIT % CELLS	O_2 CONTENT (VOL. %)	O_2 CAPACITY (VOL. %)	% SATURATION	HEMATOCRIT % CELLS	
44 Years and Under																	
H. L.	♂	42	180	23.1			53.6	95	21.8			51.5					Excision of cyst of mediastinum
W. B.	♂	27	160	17.8	18.9	94	45.8	107	18.6	20.0	93	51.2	19.0	19.1	100	50.0	Segment lower lobectomy and lingulectomy
G. C.	♂	31	160	18.4	18.6	99	47.4	55				47.8					Excision of mediastinal tumor
45 Years and Over																	
R. T.	♂	55	80	17.1				23	15.0								Inoperable carcinoma of right lower lobe
E. L.	♀	60	90	15.0	16.7	90	44.1	12	16.9	16.8	100	48.0					Inoperable exploratory thoracotomy
E. D.	♀	52	130	17.0	17.8	96	43.3	70	17.3	16.9	98	40.4					Excision of cyst of mediastinum
E. A.	♂	64	115	15.2	15.9	96	38.0	40	15.7	16.0	98	39.0					Inoperable carcinoma
Average				17.7	17.6	95	45.4	57.4	17.6	17.4	97.2	46.3					

effect of the anesthetic (ether) on these muscles. A check on the role of these factors will be presented forthwith.

Ether, the anesthesia apparatus, and the endotracheal tube can be ruled out. They are of themselves unimportant factors in the rise in carbon dioxide tension as shown in Table IX and elsewhere (Beecher, Francis, and Anfinsen[4]). Clearly (Table VIII), position is a factor in the rise of carbon dioxide tension. Other chief factors are the open pleura and depression of respiration by the anesthetic agent. These are the obvious factors. There is a curious increase in fixed acid (as shown in Table VII, B) with the passage of time. Possibly the high tensions of carbon dioxide encountered here interfere with cellular oxidations to the extent that fixed acids accumulate. The accumulation of fixed acid is puzzling, particularly in view of the failure of ether anesthesia alone to do this, as shown elsewhere.[4] The fixed acid problem is being studied further.

The statement is sometimes made that the answer to all these problems is mechanical respiration. There is perhaps still some room for doubt concerning this. For one thing, the mechanical respirators used with anesthetic agents have

TABLE VII, A. ARTERIAL BLOOD

	BEFORE OPERATION				AT OPERATION'S END			
OPERATION	NO. OF PATIENTS*	O_2 CONT. (VOL. %)	% SAT.	HEMATOCRIT % CELLS	TIME AFTER PLEURA OPEN (MIN.)	O_2 CONT. (VOL. %)	% SAT.	HEMATOCRIT % CELLS
Pneumonectomy	16	15.7	95	42	122	15.2	94	46
Lobectomy	20	16.7	95	43	95	16.3	97	45
Miscellaneous	7	17.5	95	46	58	17.5	97	46

				ALVEOLAR CO_2					ALVEOLAR CO_2	
OPERATION	NO. OF PATIENTS*	CO_2 CONT. (VOL. %)	pH	TENSION (MM. HG.)	VOL. %	TIME AFTER PLEURA OPEN (MIN.)	CO_2 CONT. (VOL. %)	pH	TENSION (MM. HG.)	VOL. %
Pneumonectomy	16	59.0	7.48	35.0	4.9	122	59.6	7.09	98.0	13.7
Lobectomy	20	57.4	7.51	32.8	4.6	95	57.9	7.22	66.6	9.3
Miscellaneous	7	58.1	7.52	32.2	4.5	58	57.4	7.37	44.0	6.2

*Not all items determined on all patients; for details see Tables I to VI.

TABLE VII, B. INCREASE IN FIXED ACID CALCULATED FROM TABLE VII, A

	Before Operation								
BEFORE	mM PER L HGB.	β	CORRECTION mM PER L	pCO_2	TOTAL CO_2 mM PER L	TOTAL $CO_2^- + .0301\ pCO_2\ [HCO_3^-]$	pH	$[HCO_3^-]$ CORRECTED TO pH 7.40	Δ A
Pneumonectomy	8.1	27.2	+1.49	35	26 6	25.5	7.48	27.0	—
Lobectomy	8.4	27.9	+2.12	33	25.9	24.9	7 51	27.0	—
Miscellaneous	8.9	29.4	+2.45	32	26.2	25.2	7.52	27.7	—
	At Operation's End								
NEAR END									
Pneumonectomy	8.9	29.4	−6 35	98	26 9	24.0	7.09	17.7	+9.3
Lobectomy	8.7	28.6	−3.61	67	26.2	24.2	7.22	20.6	+6.4
Miscellaneous	8.9	29.4	−0.62	44	25.9	24.6	7.37	24.0	+3.7

TABLE VIII. RISE IN ALVEOLAR CARBON DIOXIDE TENSION BEFORE PLEURA OPENED

PATIENT	AGE (YR.)	OPERATION	TIME AFTER ANESTHESIA STARTED (MIN.)	CHANGE IN ALVEOLAR CO_2 TENSION (MM. HG.)
B. W.	49	Pneumonectomy	30	+ 2.1
H. V.	41	Pneumonectomy	40	+16.5
A. A.	40	Lobectomy	40	+ 2.4
K. K.	54	Lobectomy	38	+15.0
F. S.	55	Lobectomy	35	+29.0
E. D.	52	Cyst (mediast.)	55	+ 6.1
R. M.	31	Lobectomy	40	+ 2.2
R. R.	55	Lobectomy	44	+19.3
C. B.	36	Pneumonectomy	60	+40.5
W. B.	27	Lobectomy	35	+13.0
[M. N.	59	Lobectomy	40	− 4.2]
Average (exclusive of last case)			42	14.6 mm. Hg. (2.0 vol. %)

TABLE IX. PATIENT SUPINE*; VARIOUS OPERATIONS (NONTHORACIC)

				BEFORE OPERATION			AT OPERATION'S END		
PATIENT	SEX	AGE (YR.)	ANESTHESIA TIME (MIN.)	pH	CO_2 (VOL. %)	CO_2 TENSION (MM. HG)	pH	CO_2 (VOL. %)	CO_2 TENSION (MM. HG)
I. S.	♀	66	255	7.45	63.6	40	7.45	60.3	39
S. T.	♀	66	195	7.45	65.6	41	7.50	57.2	33
G. F.	♀	28	170	7.38	57.3	42	7.35	49.5	38
H. M.	♀	39	95	7.37	54.1	42	7.37	52.9	41
A. G.	♂	66	93	7.40	65.6	48	7.40	58.2	42
J. B.	♂	72	87	7.35	54.1	42	7.35	50.8	40
M. S.	♀	56	120	7.40	61.3	42	7.38	59.0	41
Average				7.40	60.2	42	7.40	55.4	39

*Closed (circle filter) nitrous oxide-oxygen ether anesthesia, size 32 intratracheal tube.

proved to have a mortality rate of their own due to explosion. The unsatisfactory ventilation sometimes produced by these machines is well known. It is widely accepted that respiration carefully assisted by the anesthetist, by bag squeezing just as the patient inspires, gives the most effective type of ventilation. The following two cases, Table X, show how effective this technique is in one case (J.V.) and how unsatisfactory in the other (C.B.). However, the possible effectiveness of assisted respiration needs to be and is being studied further. In current work assistance of the respiration is started as soon as the patient is placed on his side and is continued until the chest is closed. The results of this study will be reported later, when we have had opportunity to observe an adequate number of cases.

The serious nature of the carbon dioxide tensions achieved by the end of long operations through the thorax can be inferred from the abundant evidence on this score found in man not under anesthesia. Possibly the anesthesia may afford some protection. It seems unwise to depend upon that.

Goldstein and DuBois[8] have shown that a fall of blood pressure immediately follows the cessation of rebreathing of high concentrations of carbon

TABLE X. ARTERIAL BLOOD

PATIENT	SEX	AGE (YR.)	OPERATION	BEFORE OPERATION			TIME AFTER PLEURA OPENED (MIN.)	NEAR END OPERATION			TIME AFTER PLEURA OPENED (MIN.)	AFTER ASSISTED RESPIRATION		
				CO_2 CONTENT (VOL. %)	pH	ALVEOLAR TENSION CO_2 (MM. HG)		CO_2 CONTENT (VOL. %)	pH	ALVEOLAR TENSION CO_2 (MM. HG)		CO_2 CONTENT (VOL. %)	pH	ALVEOLAR TENSION CO_2 (MM. HG)
C. B.	♂	57	Right pneumonectomy (carcinoma)	52.0	7.55	26.3	180	72.3	7.03	115.8	196	68.5	7.08	96.7
J. V.	♂	34	Left pneumonectomy (congenital cyst involving entire lung)	64.1	7.47	39.3	72	68.6	7.20	75.0	87	58.4	7.38	43.5

dioxide. Dripps[7] has discussed the fall of blood pressure which occurs when then subject is taken off cyclopropane. Under this agent he reported that the carbon dioxide tension rises to great heights; a considerable fall of blood pressure sometimes occurs when the cyclopropane is terminated. ". . . the higher the tensions of this gas (carbon dioxide) in the arterial blood the greater is the likelihood of a postanesthetic decrease in blood pressure . . ."

After the end of the surgical procedure and the change of the patient's position to a more favorable one, the pH rises and the carbon dioxide tension is reduced. The stimulant action of the carbon dioxide is withdrawn and the blood pressure falls. As pointed out previously, there is reason to believe that this is a true cause and effect relationship.

The relevance of these findings to the fall of blood pressure often found at the end of thoracic surgical procedures is quite unproved, of course, but a true relationship is probable.

Experience has shown that one can usually "get away" with patients in the position generally used (operated lung uppermost); with only occasionally assisted respiration, what appear to be satisfactory results can be obtained. The disturbing inference remains that the occasional bad results mentioned at the beginning of this paper may in some cases be directly related to the high carbon dioxide tensions reported here.

Possibly surgeons working through the open thorax may decide that they prefer to accept the real hazards of the high carbon dioxide tensions mentioned, tensions that arise as a consequence of common present practices. They may decide that this type of surgery in the supine or prone positions for example is more dangerous than the elevated carbon dioxide tensions. Such a matter is beyond our competence to decide.

In conclusion, reconsideration must be given to what constitutes the truly optimum position for operation in these cases. Equally clearly, more study based on data obtained in man must be given to effective means of assisting respiration during thoracic surgery.

SUMMARY

The blood gases, oxygen and carbon dioxide, the pH and the hematocrit value were measured before anesthesia and at intervals during surgery through the open pleura, and in some instances on the day following operation. Forty-three patients were studied. All of them received nitrous oxide-oxygen ether anesthesia.

Of the two great problems, oxygen supply and carbon dioxide removal, it was found that the techniques employed were adequate to provide oxygen but not to remove carbon dioxide. This gas rises to dangerous tensions with the passage of time. Even though the actual carbon dioxide content does not increase. the rise in tension is effected by a serious fall in pH. Various factors of possible importance in the rise of carbon dioxide tension are considered and discussed. The rise begins shortly after the patient is placed in the lateral position and before the pleura is opened. It continues with increasing rapidity (see Fig. 1).

It is shown (Table IX) that ether anesthesia, the closed anesthesia apparatus, and the endotracheal tube are not responsible, for no such rise occurs when these same factors are present in patients in the supine position. (It can be observed Table IX, that contrary to the statements made in nearly all textbooks of pharmacology, ether does not cause clinical acidosis.) Attention is called to a probable relationship between the high carbon dioxide tensions and the sudden fall of blood pressure with occasional fatality at the end of operation. In conclusion, further consideration should be given to what constitutes the optimum position for surgery in transthoracic procedures and to effective ways of assisting the respiration.

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DISCUSSION

DR. JOHN H. GIBBON, JR., Philadelphia.—This presentation interests me very much, and I think Dr. Beecher is to be congratulated on making this very careful study. I only rise to comment about it with the hope that perhaps he will try mechanical respiration and see whether it alters the acidosis which he observed. Since Crafoord, ten years ago, first talked about using a mechanical apparatus to ventilate the lungs in the presence of an open thorax, we have been interested in the method. Dr. Mautz of Cleveland has constructed a simpler apparatus for the same purpose. Last November we obtained Dr. Mautz'

apparatus through his kindness, and we also have the latest model of Crafoord's machine from Stockholm. Since then we have used these two machines on 76 patients; 66 of these had thoracotomies and 10 had upper abdominal operations.

I hope Dr. Beecher will mention some of the difficulties of blood gas determinations in the presence of ether anesthesia. We have made arterial blood gas determinations with open thoracotomies using sodium pentothal curare anesthesia without any ether. The operations were from two to five hours' duration. A needle was inserted in the brachial artery under local anesthesia. A blood sample was taken before the general anesthetic was started. Other samples were taken during, and just at the end of, the operation. With the Mautz machine, we had a significant rise in arterial CO_2 tension in only 1 case out of 5. In 6 of the 9 cases in which we used Crafoord's machine, there was a slight rise, but not to the extent Dr. Beecher reported.

I hope Dr. Beecher will try mechanical respiration and repeat his observations. Unfortunately, we have no arterial blood gas studies without mechanical respiration to compare with the results we have just mentioned.

Finally, I think it is fair to point out, as Dr. Beecher has emphasized, that once an increase in alveolar CO_2 tension occurs it is rather difficult to reduce it. In one case he was successful and in the other not so successful. I think what we all want to do is to avoid getting the increase if we possibly can. I think this is a very interesting work, and I hope the study will be continued.

DR. BEECHER.—I would like to thank Dr. Gibbon for his remarks, and to say that the question he raised about measuring blood gas in the presence of ether is a fairly technical business, and I should like to discuss it outside the meeting as I do not believe it would interest enough of those here. I wondered if in his cases he had taken the blood, where he found a relatively small rise, before the mask was removed. Some of the CO_2 elevations will adjust themselves very rapidly and others take a considerable period of time.

I did not mean to imply that we had a closed mind about any ways of improving this situation. I am very sure, from the fact that these CO_2 tensions begin to rise before the pleura is opened when the respiratory minute volume and rate seem to be within quite reasonable limits, that a normal type of respiration is not the whole answer to correcting this difficulty. I still think it would be desirable for surgeons to consider the possibility of other operating positions for these cases. We anesthetists on our side must find improved ways of assisting respiration in these cases—improvements based upon determinations of arterial oxygen and CO_2 and pH.

BLOOD VOLUME CHANGES IN TUBERCULOUS PATIENTS TREATED BY THORACOPLASTY

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THE patient with pulmonary tuberculosis, when presented for thoracoplasty, frequently has lost weight, is anemic, and has had prolonged pulmonary suppuration. The circulating blood volume, the total plasma protein, and total hemoglobin are rarely measured although a diminished blood volume in debilitated patients has been noted by Clark,[2] Gregersen,[10] and Varco.[18] Though it would be suspected that patients with far-advanced pulmonary tuberculosis would fall into this group of patients, staged thoracoplasty is generally well tolerated.

We have found occasional patients who did not tolerate thoracoplasty well, and have been forced by a rising pulse rate or falling blood pressure to terminate the procedure before the desired collapse was obtained. This has occurred despite the fact that the blood lost during the operative procedure was adequately replaced. This occurred more frequently during the second and third stages of thoracoplasty. A reduced blood volume might account for this. To obtain pertinent data, preoperative blood volumes were determined, blood loss at operation was measured, and blood loss between stages of thoracoplasty was determined. The last determination has received little attention, and it occurred to us this additional drain on a depleted blood volume might account for the frequency of shock in the later stages of thoracoplasty.

No reference in the literature to changes in blood volume in patients with pulmonary tuberculosis was found. Blood loss during thoracoplasty and other thoracic procedures has been reported. Stewart and Rourke,[14] using the acid hematin method of blood loss determination of Gatch and Little,[6] found the blood loss in four thoracoplasties varied from 400 to 900 c.c. Neither the disease of the patient nor the stage or extent of the thoracoplasty was stated. White and Buxton,[17] using the same method, estimated an average 700 c.c. blood loss with each of the three stages of thoracoplasty, but no attempt was made to determine blood lost in the interval between the stages.

Thomas, Adams, and Thornton,[15] in their study of blood volume changes following intrathoracic operations, made no exact measurement of blood loss at the time of operation in most instances. However, in five nontuberculous cases they did determine the blood volume before and after operation using the method of Gibson and Evans[7] adapted to the photoelectric microcolorimeter by Gibson and Evelyn.[9] After determining the erythrocyte count, hemoglobin, hematocrit value, plasma protein concentration pre- and postoperatively, and the surgeon's estimate of the blood loss, they came to the conclusion that from

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a practical standpoint the hematocrit reading was the most valuable index in the determination of blood loss and blood replacement. Ebert, Stead, and Gibson,[5] in studying the response of normal subjects to acute blood loss, reported that the hematocrit reflected the direction of changes in plasma volume. Stewart and Rourke[14] found no relationship between changes in the hematocrit value, hemoglobin, plasma protein, and the amount of blood lost. They concluded that these determinations should not be used as criteria for fluid replacement. Coller, Crook, and Iob,[3] have corroborated their findings.

METHOD

Blood lost at operation was determined by two methods. All sponges were weighed before and immediately after use as described by Wangensteen,[1, 16] and weights were determined to the nearest 0.1 Gm. The difference in weight was taken to represent the weight of blood lost. Blood volume determinations were made before and after operation using the method of Gibson and Evans[7] as modified by Gibson and Evelyn[9] for use with a photoelectric microcolorimeter. The blood was drawn without stasis from a large vein in the arm, usually the median antecubital. The syringe was then removed and the needle left in the vein. A known amount of Evans blue dye T-1824 in a calibrated syringe was immediately injected through this same needle. Blood samples were taken 8, 10, 12, and 14 minutes after injection of the dye. The blood was allowed to clot and then was centrifuged at 2,000 r.p.m. for 15 minutes. Specimens showing hemolysis were discarded. The serum containing the dye was drawn off by pipette, and a little over 1 c.c. was placed in a micro-absorption cell of the plunger type, and light absorption was determined in the Evelyn colorimeter using a 620 mμ filter. Light absorption of the same specimen when using a 540 mμ filter was then determined to correct for unrecognized hemolysis. The galvanometer reading made with the 620 mμ filter was then corrected. The corrected galvanometer readings were then plotted against the time the dye samples were taken, and the galvanometer readings extrapolated to zero time were used to calculate the plasma volume. The blood volume was calculated from the hematocrit and plasma volume. Plasma protein concentration was determined by the copper sulfate method of Phillips and associates.[13] Total circulating plasma protein concentration was calculated from the plasma volume and protein concentration.

The procedure used in the present series is identical with that described by Miller, Gibbon, and Allbritten[12] in this laboratory. The standard error of estimation as determined by Miller and associates[12] was the same. It was determined by noting the difference between repeat determinations of blood volumes in twenty-five subjects. The repeated determinations were done on each subject within a twenty-four hour period. The differences lay between 0.4 and 7 per cent. The mean experimental difference was 4 per cent. The standard error of estimation was ± 176 c.c. The preoperative blood volume determination was made the day preceding operation. The postoperative blood volume studies were carried out within 30 minutes after completion of the operation. No patient was in shock. Blood loss was calculated by adding the amount of blood given during operation to the preoperative blood volume and subtracting the postoperative blood volume from the sum.

The amount of blood lost between operative procedures was estimated by determining the difference between the postoperative blood volume of any given stage and the preoperative blood volume of the following stage of thoracoplasty and adding the amount of blood transfused during the same interval.

RESULTS

Observations were made on ten patients with pulmonary tuberculosis treated by thoracoplasty. These consisted first, of body weight changes that occurred prior to entering the surgical service; second, the amount of blood lost during

and between the stages of thoracoplasty; third, the amount of blood needed to replace operative and interval loss; and finally the changes that occurred in the hematocrit reading and total circulating plasma protein as a result of each stage of thoracoplasty.

Using normal standards of sex, weight, height, and age[5] as a basis for estimation, three of the ten patients studied were of normal or greater than normal weight; seven patients were 8 to 33 pounds underweight. All had far-advanced pulmonary tuberculosis. Five patients had unilateral disease, and five patients had bilateral disease with a contralateral pneumothorax.

Using the chart of Gibson and Evans[9] to calculate the expected blood volume from the surface area of the patient, all except one patient had a decreased circulating blood volume when admitted to the surgical service. The minimum decrease was 4.5 per cent and maximum decrease 27.5 per cent, and the average was 15.6 per cent below the blood volume expected. Clark and associates[2] stated that the blood deficit should be calculated on the basis of usual weight prior to illness. If the expected blood volume had been estimated from a surface area calculated from the normal weight for the patient's sex, height, and age,[4] the minimum decrease would have been 4.7 per cent, the maximum 36.9 per cent, and the average decrease 18.5 per cent.

The blood loss during a first stage thoracoplasty averaged approximately 830 c.c., during a second stage, 480 c.c., and during a third stage, 400 c.c. These sums represent the difference between the preoperative and postoperative blood volume (Table I). When determined by the sponge weight method, the blood loss averaged 850 c.c. for a first stage, 400 c.c. loss for a second stage, and 260 c.c. for a third stage of thoracoplasty. The correlation between the two methods of determining operative blood loss is shown in Fig. 1.

TABLE I. ESTIMATED BLOOD LOSS DURING STAGES OF THORACOPLASTY

		BY WEIGHING SPONGES (C.C. BLOOD)				BY DYE METHOD (C.C. BLOOD)		
STAGES	CASES	MINIMUM	MAXIMUM	AVERAGE	CASES	MINIMUM	MAXIMUM	AVERAGE
First	8	467	1407	855	10	419	1558	832
Second	10	110	990	404	10	95	958	480
Third	5	97	493	262	7	76	858	397

The average total operative blood loss when determined by differences in blood volume for those patients undergoing three stages of thoracoplasty was 1,670 c.c., and 1,430 c.c. when estimated by sponge weight method (Table II). The average operative loss for those patients who had a two-stage, seven-rib thoracoplasty was 1,520 c.c. as determined by the dye T-1824 method, while operative loss estimated by weighing the sponges was 1,220 c.c. (Table III).

The blood loss between the first and second stages of thoracoplasty averaged 430 c.c. and in the interval between the second and third stages this loss averaged 702 c.c. (Table IV). This figure includes the blood lost by one patient (C. K.) by an excessive hemorrhage after the operation. If this figure is eliminated, the

average loss between the second and third stages is 445 c.c. There was no significant blood loss between the third stage and the time of discharge, while the average blood loss between the second stage and the time of discharge in the patients who had only two stages of thoracoplasty was 418 c.c. (Table V).

The operative blood loss was inadequately replaced at the time of operation in four instances by amounts varying from 260 to 460 c.c. Three of these four patients received transfusions of blood upon return to their room. Most patients received interval transfusions to replace loss of blood into the extrafascial space in the interval between operations.

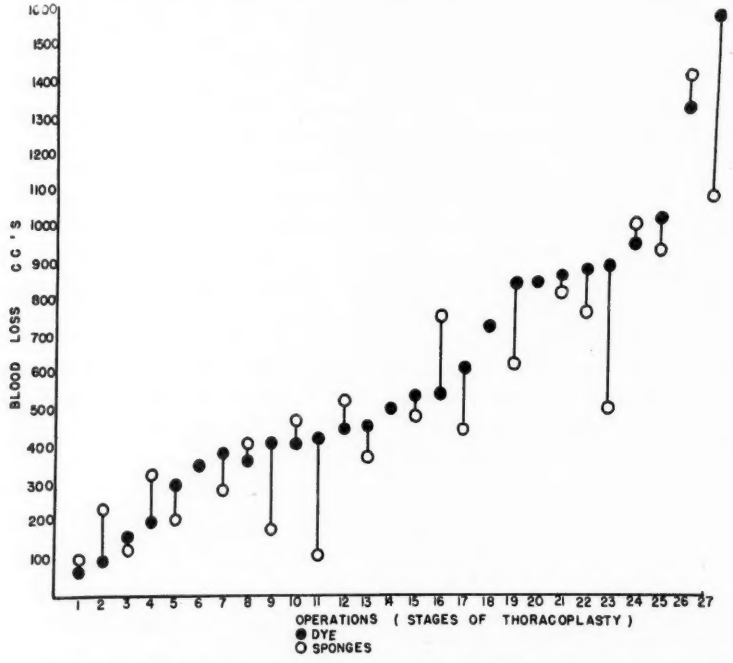

Fig. 1.—Comparison of blood loss as determined by sponge-weighing method and dye (T-1824) method as observed in stages of thoracoplasty.

Hematocrit and total circulating plasma protein concentration showed a trend only suggesting blood deficiency or overreplacement (Figs. 2 and 3). Variations were too great to use these as a basis for accurate estimate of blood lost or blood overreplaced in individual instances.

A miscellaneous group of eleven patients were followed from three months to one year after thoracoplasty. Five patients with arrested disease had gained weight, and the blood volumes had risen to a level nearly equal to the expected blood volume for the surface area. Of these five patients, one had bilateral tuberculosis with contralateral pneumothorax and four had unilateral tubercu-

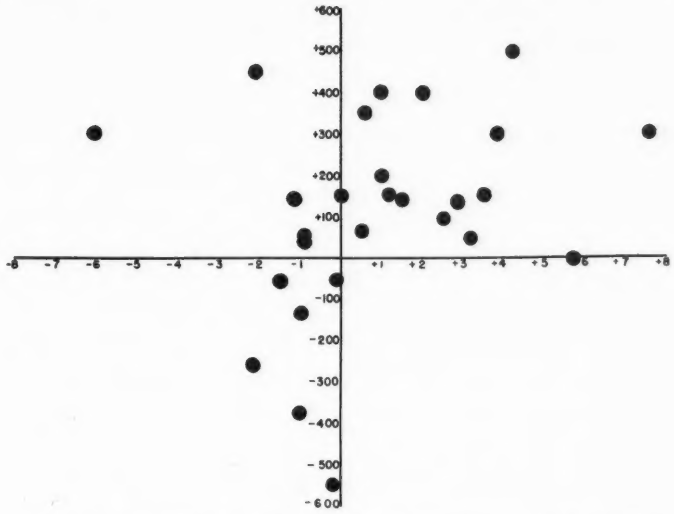

Fig. 2.—Relation of changes in hematocrit to overreplacement and underreplacement of blood at each stage of thoracoplasty. The increase or decrease in hematocrit is the abscissa, and the overreplacement or underreplacement of the blood is the ordinate in the graph.

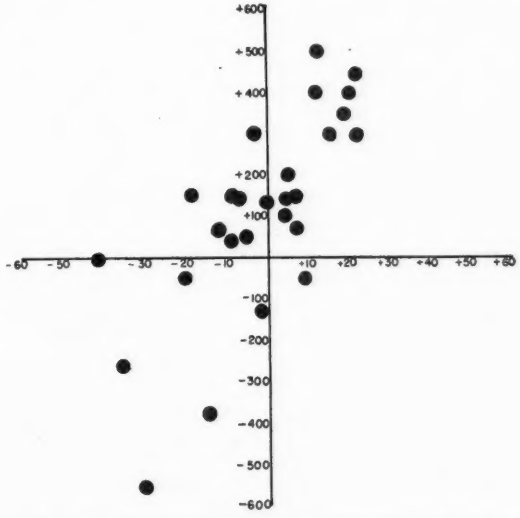

Fig. 3.—The relation of changes in total circulating plasma protein to overreplacement or underreplacement of blood at each stage of thoracoplasty. The increase in grams in the total circulating plasma protein is charted as the abscissa, and the blood replacement in cubic centimeters is charted as the ordinate.

TABLE II. TOTAL OPERATIVE BLOOD LOSS FOR SEVEN RIB THORACOPLASTY COMPLETED IN THREE STAGES

CASES	ESTIMATED BY WEIGHING SPONGES		CASES	ESTIMATED BY DYE METHOD	
3	Minimum	1156	7	Minimum	1019
	Maximum	1776		Maximum	2672
	Average	1427		Average	1674

TABLE III. TOTAL OPERATIVE BLOOD LOSS FOR SEVEN RIB THORACOPLASTY COMPLETED IN TWO STAGES

CASES		ESTIMATED BY WEIGHING SPONGES	ESTIMATED BY DYE METHOD
3	Minimum	967	1313
	Maximum	1410	1767
	Average	1223	1523

TABLE IV. INTERVAL BLOOD LOSS BETWEEN STAGES

	BETWEEN FIRST AND SECOND STAGES IN 10 CASES (C.C.)	BETWEEN SECOND AND THIRD STAGES IN 7 CASES (C.C.)
Minimum	+14	+254
Maximum	991	2241*
Average	428	702 (445)†

*Includes blood loss of patient (C.K.) who had excessive hemorrhage.
†Excludes blood loss of (C.K.).

TABLE V. INTERVAL BLOOD LOSS BETWEEN LAST OPERATION AND DISCHARGE

	BETWEEN SECOND STAGE AND DISCHARGE IN 3 CASES (C.C.)	BETWEEN THIRD STAGE AND DISCHARGE IN 7 CASES (C.C.)
Minimum	203	+736
Maximum	725	543
Average	418	+10

TABLE VI. CALCULATED TOTAL INTERVAL LOSS

CASES	THREE STAGES		CASES	TWO STAGES	
6	Minimum	517	3	Minimum	771
	Maximum	1078		Maximum	1025
	Average	830*		Average	884

*Interval blood loss of patient (C.K.) eliminated because of excessive interval hemorrhage.

TABLE VII. TOTAL BLOOD LOSS DURING THORACOPLASTY

CASES	THREE STAGES		CASES	TWO STAGES	
6	Minimum	1934	3	Minimum	2168
	Maximum	2984		Maximum	2792
	Average	2385*		Average	2407

*Interval blood loss of patient (C.K.) eliminated because of excessive interval hemorrhage.

losis. The other six patients still had active pulmonary tuberculosis. These six patients had not gained weight, and the blood volumes had not increased above the preoperative figures.

DISCUSSION

It has been pointed out by several investigators, Clark and associates,[2] Gregersen,[10] and Varco,[18] that a patient with chronic illness generally has a decreased circulating blood volume. In ten patients with pulmonary tuberculosis, it was observed that although the weight of three of the patients was normal,

or above normal, the blood volume was decreased in all but one, and, when estimated by surface area, averaged 15.6 per cent below the expected figure. Seven of the patients had lost weight, and two of the patients required repeated blood transfusions before thoracoplasty could be started. Clark and associates[2] stated that correction of blood volume deficits by transfusion has proved to be the most important single factor in the preparation of such patients for surgery. Blood replacement during the operation and in the intervals between the stages of thoracoplasty is equally important. It is during these intervals between the stages that an unrecognized loss of serosanguineous fluid into the operative wound space occurred. The long posterolateral incision, multiple periosteal incisions, and the creation of a large extrafascial space are all conducive to exudation. The space created by the resection of the upper three to five ribs remains until obliterated by subsequent operative procedures. Although it was known that blood and fluid did extravasate into the space, it was thought to be of little consequence. The results of these determinations showed that the amount of blood lost in this manner is significant and that chronically ill patients undergoing a multiple staged operative procedure will be aided by the replacement of the blood lost during that time. Though blood loss at operation was adequately replaced, occasionally thoracoplasty had to be discontinued after giving the anesthetic, for the pulse rate rose and the blood pressure decreased beyond an acceptable point. This occurred more commonly in patients with far-advanced bilateral disease and in the second and third stages of thoracoplasty.

Corroborating the work of Stewart and Rourke[14] and Coller and associates,[3] it was found that neither the hematocrit nor the total circulating plasma protein were reliable indices of the need of blood replacement. Griffin and associates,[11] also found that the plasma volume and the total circulating plasma albumin varied so widely in normal individuals that they were of no value in estimating dehydration or protein depletion in patients with malnutrition.

Clark and associates[2] stated that restoration of the blood volume preceded significant recovery of weight during recuperation from debilitating illness. Our results corroborated this statement. Patients with quiescent or arrested disease have shown a return of their blood volumes to a normal range, a weight increase, and a tolerance for mild exercise. In those patients with persistent active disease the blood volume remained low or decreased.

SUMMARY

1. Ten patients with pulmonary tuberculosis had a decreased blood volume upon their admission to the surgical service.

2. Blood lost during the stages of thoracoplasty was measured by the sponge weight method and calculated by differences in circulating blood volumes before and after operation.

3. There is a significant loss of blood between stages of thoracoplasty.

4. Blood replacement is required at the time of operation and during the interval between the stages of thoracoplasty to maintain an optimum blood volume.

5. Neither the hematocrit nor the total circulating plasma protein is an accurate indicator of the amount of blood lost or replaced.

6. An increase in the circulating blood volume of the patients studied paralleled their general clinical improvement.

The technical assistance of Mr. Franz Goldstein is gratefully acknowledged.

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DISCUSSION

DR. D. H. WATERMAN, Knoxville, Tenn.—To my mind this is a highly significant paper, and one I do not wish to let go without discussion. In spite of the dramatic things that are occurring in thoracic surgery, we must not lose sight of the fact that thoracoplasty is the common operation that we are doing day in and day out, and that the excellent data Dr. Allbritten and his associates have presented certainly point the way to more adequate management of this large group of patients.

I trust there are no longer thoracic surgeons who pride themselves on never using transfusion in thoracoplasty; some years ago that was a not uncommon attitude. I am sure that all of us now routinely use transfusion in every case of thoracoplasty, and that many of us are coming to the point of giving a transfusion in the interval between stages as well.

I might mention that in our own series we have routinely, in the last 100 cases of thoracoplasty, given two pints of blood at the first stage and one at each of the succeeding stages, with quite a large percentage of patients now receiving another 500 c.c. transfusion in the interval. I am happy to see that these data have confirmed the clinical impressions we have had that there must be a further blood loss during this interval. I wish again to congratulate Dr. Allbritten on this study.

DR. EMILE HOLMAN, San Francisco.—I too wish to congratulate the speaker on these significant findings. I thought you might be interested in a little indirect evidence of the decreased blood volume in these patients. (Slides.)

You are all acquainted with the change in size of the heart that corresponds with blood loss imposed on a dog, for example; this is the normal heart size. Remove 300 c.c. of blood and we have a heart that is correspondingly smaller; remove 300 c.c. more blood and the heart becomes even smaller. Restore the blood and it is a little larger than the original heart, because in the meantime the circulating blood has been increased by accretions from the blood reservoirs, such as the spleen and body tissues. No doubt you have all noted the very small heart (slides) in the presence of pulmonary tuberculosis, which we have been ascribing to a decreased blood volume. About ten years ago a young Chinese doctor, Chang, studied the blood volume in tuberculous patients in our clinic. Unfortunately, probably due to the limitations of the method used, they all turned out normal. The studies this morning indicate that our thesis was sound, and that the small heart noted in tuberculous patients may be considered indirect evidence of a decreased blood volume in these patients.

DR. ADRIAN LAMBERT, New York.—I have been interested in these cases that come to surgery for tuberculosis, especially in patients with tuberculous empyemas who have not been able to withstand surgery. In 1944, we had occasion to do some isolated blood volume studies and found, as Dr. Allbritten did, that their blood volumes were low. We, therefore, went about looking for blood for them, which was not available; we appealed to the Red Cross, and they gave us some red blood cells which we mixed with 10 per cent corn syrup according to the method of Thalheimer, as published by Thalheimer and Stephens. This allowed us to keep the blood viable and useful for more than thirty days, and we gave four transfusions a week for four weeks to a series of approximately ten patients on our wards who were debilitated, with chronic draining wounds. These patients, after this treatment, looked as if they had been to Florida; they were florid in complexion and underwent certain changes which were interesting. They began to gain weight, their appetites increased, and the character of their wounds changed. The granulations became pink and whereas, before, the type of suppuration and purulent material was profuse and thick, it dried up and the secretions became quite watery. We used that as a preoperative measure and thought it enabled them to withstand surgery which they were not otherwise able to do.

DR. ALLBRITTEN, JR.—I wish to thank the discussors. We are not aware of any previous determinations of circulating blood volume in patients with pulmonary tuberculosis or the amount of blood lost in the intervals between stages of thoracoplasty.

Though patients generally receive blood transfusions during thoracoplasty there is a tendency to underestimate the requirements for adequate replacement unless the approximate figures as based upon actual measurement are known.

PULMONARY CIRCULATION AND ALVEOLAR VENTILATION—PERFUSION RELATIONSHIPS AFTER PNEUMONECTOMY

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THE resection of one lung necessitates readjustments in the mechanics of the chest bellows and a redistribution of blood flow and ventilation through the remaining lung. Several problems concerning the manner in which these adaptive processes take place are of interest to the thoracic surgeon, the physiologist, and the pathologist. In three previous papers, physiologic studies have been reported on the effect of pneumonectomy in a group of 4 young children followed up to adult age[1, 2] and in a group of adults followed for a short period of time.[3] The techniques available when these reports were made included the measurements of (a) lung volumes, (b) maximum breathing capacity, (c) distribution of tidal air throughout the lung, (d) ventilation, and (e) arterial blood oxygen saturation under varying states of activity. The following tentative conclusions were reached on the basis of the data obtained with these techniques: (1) A single lung, provided it is maintained within its normal confines naturally or following a thoracoplasty, is capable of a high degree of efficiency in both the ventilatory and the respiratory aspects of pulmonary function; (2) pulmonary distention, defined as a greater than normal size of the remaining lung in forced expiration, is not functionally desirable in young and adult subjects as it limits the ventilatory capacity of the chest bellows and causes a reduction in the arterial oxygen saturation during a severe type of exercise; and (3) fixation of the mediastinal contents in their normal position, following the use of pneumothorax, oleothorax, or thoracoplasty corrects the latter disturbances. Birath,[4] who was concerned chiefly with the ventilatory aspects of the adaptation, has since confirmed that a distended lung loses some of its efficiency in distributing tidal air. Since these studies were undertaken two new methods have been introduced in clinical investigation; that is, cardiac catheterization[4] and the measurement of partial pressures of carbon dioxide and oxygen in the arterial blood,[5, 6] which methods might give interesting information regarding the effect of pneumonectomy upon the pulmonary ventilation and circulation. With the cardiac catheterization technique, it is possible to study the variation in pulmonary blood flow and pulmonary arterial pressure[7, 8, 9] at rest and during a steady state of moderate exercise. By combining the data obtained from the measurement of partial pressures of carbon dioxide and oxygen in arterial blood with some of the data obtained by catheterization of the heart the relationships existing between alveolar ventilation and perfusion of pulmonary capillaries may be

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closely investigated.[10] The measurement of partial pressures of oxygen in the arterial blood is a more sensitive index of the state of oxygenation of the arterial blood than the measurement of the oxygen saturation, because of the characteristics of the oxyhemoglobin dissociation curve as it approaches full oxygen saturation. The studies to be reported in this paper are based upon analyses of the data obtained with both these methods and also with the methods previously used. The 16 cases which were investigated offer a great diversity with regard to the nature of the pathologic process prior to pulmonary resection, the time interval after pneumonectomy, the age of the subject, and the presence or absence of a thoracoplasty.

MATERIAL FOR STUDY

The 16 cases which form the basis of this report may be divided into two groups. A first group (Group I) of 7 patients was studied within the first five months following pneumonectomy, and a second group (Group II) of 9 patients was studied from 25 to 131 months after pneumonectomy.

In Tables I and II are summarized the physical characteristics and the essential clinical data at the time of the latest study.

TABLE I. PHYSICAL CHARACTERISTICS AND CLINICAL DATA IN A GROUP OF 7 CASES STUDIED WITHIN A FEW MONTHS AFTER PNEUMONECTOMY (GROUP I)

SUBJECT	AGE (YR.)	SEX	WEIGHT (KG.)	HEIGHT (CM.)	BODY SURFACE AREA (SQ. M.)	DIAGNOSIS	DATE OF RESECTION	DATE OF STUDIES
G. H.	48	M	65	177	1.81	Bronchiectasis, left pneumonectomy, no thoracoplasty	4/ 9/48	5/12/48
V. Ab.	35	M	72	171	1.83	Bronchiectasis, bilateral pulmonary emphysema; right pneumonectomy, no thoracoplasty	6/27/47	6/12/47 10/14/47
A. Am.	24	M	75	169	1.86	Bronchiectasis, left pneumonectomy, thoracoplasty, no scoliosis	10/20/47	10/ 2/47 1/22/48
C. Ro.	22	F	50	150	1.43	Tubercular stenosis of left bronchus, left pneumonectomy, thoracoplasty no scoliosis	5/ 7/47	6/17/47
J. Ra.	15	M	54	164	1.59	Tubercular stenosis of right bronchus, right pneumonectomy, thoracoplasty, no scoliosis	5/18/48	11/10/48
C. McL.	34	M	44	166	1.46	Bronchiectasis, right pneumonectomy, thoracoplasty, scoliosis	8/ 6/47	1/20/48
J. Rut.	57	M	54	157	1.53	Bronchiectasis, lung abscess, left pneumonectomy, thoracoplasty, scoliosis	6/28/48	6/ 2/48 9/27/48

TABLE II. PHYSICAL CHARACTERISTICS AND CLINICAL DATA IN A GROUP OF 9 CASES STUDIED SEVERAL YEARS AFTER PNEUMONECTOMY (GROUP II)

SUBJECT	AGE (YR.)	SEX	WEIGHT (KG.)	HEIGHT (CM.)	BODY SURFACE AREA (SQ. M.)	DIAGNOSIS	DATE OF RESECTION	DATE OF STUDIES
H. W.*	17	F	59	165	1.65	Bronchiectasis, left pneumonectomy, no thoracoplasty	10/ 5/37	11/10/48 2/15/49
R. G.*	21	M	63	177	1.78	Bronchiectasis, left pneumonectomy, no thoracoplasty	2/18/38	12/19/47
S. R.	41	M	80	173	1.93	Lung abscess (foreign body), right pneumonectomy, no thoracoplasty	11/15/45	12/17/47
J. Lo.*	19	M	66	171	1.78	Bronchiectasis, left pneumonectomy, no thoracoplasty; pulmonary distention	11/10/39	9/21/48
J. Rus.	61‡	M	46	158	1.44	Squamous-cell bronchial carcinoma, right pneumonectomy, no thoracoplasty, nonobstructive pulmonary emphysema	2/27/46	4/ 1/46 5/ 5/48
V. Wat.	72‡	M	65	175	1.79	Oat-cell bronchial carcinoma, left pneumonectomy, no thoracoplasty, nonobstructive pulmonary emphysema, systemic arterial hypertension	8/ 2/41	12/12/41 1/26/44 9/18/44 9/ 7/48
D. M.†	66	M	62	179	1.79	Transitional cell bronchial carcinoma, bilateral obstructive emphysema, arteriosclerotic heart disease, left pneumonectomy, no thoracoplasty	11/23/40	12/15/41 2/23/44
E. Re.†	39‡	M	53	175	1.64	Bronchiectasis, left pneumonectomy, thoracoplasty, no scoliosis, bronchiectasis right middle lobe, slight pulmonary distention	7/18/41	3/18/48
F. I.†	53‡	M	69	178	1.86	Tubercular stenosis of right bronchus, right pneumonectomy, thoracoplasty, slight pulmonary distention, mild systemic arterial hypertension	5/19/41	8/10/42 12/13/48

*Cases reported in J. THORACIC SURG. **16**: 30, 1947, under same initials.
†Cases reported in Ann. Surg. **116**: 532, 1942, under same initials.
‡Age at time of latest study.

METHODS

1. The following measurements were made routinely in the 16 cases and were usually repeated at intervals in the 9 cases of the second group: (a) Lung volume and maximum breathing capacity; (b) pulmonary emptying rate or index of intrapulmonary mixing; (c) ventilation and gas exchange at rest, during a standard exercise test of one minute's duration, and during the first five minutes of recovery following the exercise. The techniques used in these routine studies have been described in detail recently.[11] In the same report may be found standard values for normal individuals, which vary with age, sex, and body size.

2. The study of the relationships between alveolar ventilation and alveolar perfusion was based on techniques recently developed, and on a physiologic interpretation of the data obtained by these techniques. The techniques consist of: (a) The collection of blood samples from the brachial artery through an indwelling needle and the determination in these samples of the carbon dioxide (pCO_2) and oxygen (pO_2) tensions by the bubble technique developed by Riley and associates;[5] (b) the simultaneous collection of mixed venous blood samples using the technique of cardiac catheterization and the determination of O_2 content and the O_2 saturation in these samples; (c) the simultaneous measurement of the ventilation and of the CO_2 output and O_2 intake from which the respiratory quotient may be calculated. These measurements are made at rest, under basal conditions and during the steady state attained after ten to twelve minutes of a moderate exercise with the subject breathing room air. The exercise was of two types: a leg exercise with the subject in the recumbent position, flat on his back, and/or a bicycle exercise.

On the basis of physiologic concepts developed by Lilienthal and co-workers[6] and more recently expanded by Riley and Cournand,[10] the data obtained by these techniques may be used to analyze the ventilation-perfusion relationships in the lungs starting with the concept of "ideal" alveolar oxygen and carbon dioxide tensions. These ideal tensions are those which the alveolar air and the blood leaving the pulmonary capillaries would have if there were homogeneous ventilation and perfusion of the alveoli throughout the lungs and if the gas tensions in the alveolar air and in the capillary blood reached perfect equilibrium. The "ideal" alveolo-arterial pO_2 gradient results chiefly from the fact that all alveoli do not contain "ideal" alveolar air because the ventilation-perfusion relationships vary.

To facilitate the quantitative analysis of ventilation-perfusion relationships, all pulmonary alveoli may be considered as if they fell into one of three categories: (1) "ideal" alveoli with "ideal" ventilation-perfusion relationships ("ideal" pO_2 and pCO_2); (2) alveoli which are perfused but not ventilated (mixed venous blood partial pressures); and (3) alveoli which are ventilated but not perfused (inspired air partial pressures). If total pulmonary blood flow (cardiac output) is known, it is then possible to calculate the effective pulmonary blood flow, which is the portion of total pulmonary blood flow perfusing "ideal" alveoli. The ratio of effective pulmonary blood flow to total pulmonary blood flow in the absence of a true shunt provides a quantitative estimate of the

physiologic importance of alveoli which are well perfused but poorly ventilated. If total ventilation is known, it is possible to calculate the effective alveolar ventilation, which is that portion of total ventilation distributed to "ideal" alveoli. The ratio of effective alveolar ventilation to total ventilation provides a quantitative estimate of the physiologic importance of alveoli which are well ventilated but poorly perfused.

A schematic representation of these relationships is given in Fig. 1, in which ventilation is considered as a continuous process.

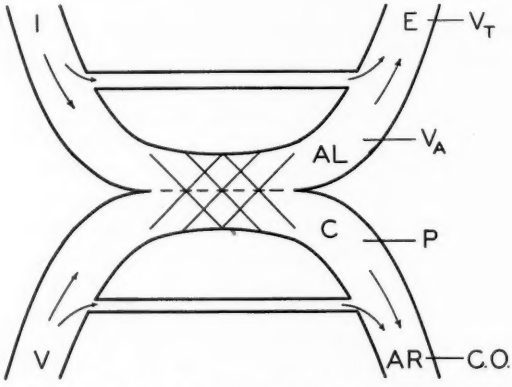

Fig. 1.—Schematic representation of ventilation, perfusion, and gas exchange.[10]

The symbols represent

a. The composition of respiratory gas (partial pressure or content): in *I*, inspired air; *E*, expired air; *V*, mixed venous blood; *Ar*, arterial blood; *Al*, "ideal" alveolar air; *C*, blood leaving "ideal" alveoli.

b. The rate of flow in liters per minute: V_A effective ventilation; *P*, effective pulmonary blood flow; *VT*, total ventilation; *CO*, total pulmonary blood flow.

The volume of gas, with the composition of inspired air, bypassing the "ideal" alveoli, is influenced by the anatomic size of the bronchial tree, the gaseous diffusion between terminal bronchioles and alveoli, and the proportion of poorly perfused or nonperfused alveoli.

The volume of blood with the composition of mixed venus blood by-passing the "ideal" capillaries is influenced by the proportion of poorly ventilated or nonventilated alveoli.

In normal individuals effective pulmonary blood flow constitutes at least 94 per cent of total pulmonary blood flow and the effective alveolar ventilation constitutes at least 70 per cent of total ventilation.

Deviations from these normal percentage figures, in the absence of technical errors, are of three types, the description and interpretation of which follows:

1. A reduction of both effective pulmonary blood flow and effective alveolar ventilation below the normal percentage indicates abnormalities of distribution of ventilation and perfusion throughout the lungs, the extent of which is determined by the calculated percentage.
2. A reduction of the effective pulmonary blood flow below the normal percentage, combined with an effective alveolar ventilation within the normal percentage range, indicates either passage of blood through totally unventilated portions of the lungs (true shunt) or circulation through poorly ventilated alveoli.

3. A reduction of the effective alveolar ventilation below the normal percentage combined with an effective pulmonary blood flow within the normal percentage range indicates restriction of the circulation through well-ventilated parts of the lungs.

The following formulas were used in these calculations:

1. $$\text{"Ideal" alv. } pO_2 = \text{Insp. } pO_{2c} - \frac{\text{Art. } pCO_2}{\text{R.Q.}}$$

where

"Ideal" alv. pO_2 = "Ideal" alveolar oxygen tension in mm. Hg
Insp. pO_{2c} = partial pressure of oxygen in inspired air in mm. Hg corrected for difference in volume between inspired air and alveolar air
Art. pCO_2 = Arterial blood carbon dioxide partial pressure in mm. Hg
R.Q. = Respiratory quotient

2. $$\text{E.P.B.F.} = \text{T.P.B.F.} \times \left[1 - \frac{X - AR}{X - MVB}\right]$$

where

E.P.B.F. = Effective pulmonary blood flow in liters per minute per m^2 B.S.
T.P.B.F. = Total pulmonary blood flow in liters per minute per m^2 B.S.
X = "Ideal" capillary blood O_2 saturation per cent
AR = Arterial blood oxygen saturation per cent
MVB = Mixed venous blood oxygen saturation per cent

3. $$\text{Alv. Vent.} = \text{Tot. Vent.} \times \left[1 - \frac{\text{Art. } pCO_2 - \text{Exp. } pCO_2}{\text{Art. } pCO_2}\right]$$

where

Alv. Vent. = Alveolar ventilation in liters per minute per m^2 B.S.
Tot. Vent. = Total ventilation in liters per minute per m^2 B.S. corrected for the effect of apparatus dead space
Art. pCO_2 = Arterial carbon dioxide partial pressure in mm. Hg
Exp. pCO_2 = Expired carbon dioxide partial pressure in mm. Hg

Studies were also performed with the subjects at rest, breathing a mixture of approximately 12 per cent oxygen in nitrogen. Contrary to the situation which obtains during breathing of room air, nearly perfect equilibrium between alveolar pO_2 and the pO_2 of the blood leaving the alveolar capillaries is not reached during low oxygen breathing. Under these circumstances the alveolo-arterial pO_2 gradient is related chiefly to the diffusion characteristics of the tissue-fluid barrier (the "pulmonary membrane") between the blood and gas phases. In normal individuals this gradient is below 12 mm. Hg. From this gradient the diffusion constant for the lung as a whole can be estimated.

RESULTS

The results in the two groups will be discussed separately.

Group I

The data obtained from the 7 patients of this group are tabulated in Tables III, IV, V, VI, VII, XII, XIV, and XV, and may be compared in these tables with normal or predicted values. Measurements were made only once between

TABLE III. LUNG VOLUMES AND MAXIMUM BREATHING CAPACITY IN 7 CASES STUDIED WITHIN A FEW MONTHS AFTER PNEUMONECTOMY (GROUP I)

SUBJECT	TIME AFTER OPERATION (MO.)	VITAL CAPACITY (IN C.C.)		RESIDUAL AIR (IN C.C.)		TOTAL CAPACITY (IN C.C.)		RESIDUAL AIR / TOTAL CAPACITY × 100		MAXIMUM BREATHING CAPACITY (LITERS)	
		PREDICTED*	OBSERVED	PREDICTED*	OBSERVED	PREDICTED*	OBSERVED	PREDICTED	OBSERVED	PREDICTED†	OBSERVED
G. H.	1	2160	1905	660	785	2820	2690	23	28	110	92
V. Ab.	Before	4050	1360	1230	2410	5280	3770	23	64	129	41
	4	1823	1867	557	1706	2380	3573	23	48	129	40
A. Am.	Before	4200	3987	1050	1753	5250	5740	20	31	147	103
	3	2310	2565	578	576	2888	3141	20	18	147	108
C. Ro.	1½	1611	1636	403	470	2014	2106	20	22	86	73
J. Ra.	5	1915	1734	480	442	2395	2176	20	20	115	84
C. McL.	5	1776	1142	544	802	2320	1944	23	41	100	38
J. Rut.	Before	3310	2554	1475	1184	4785	3738	31	32	63	47
	3	1820	1701	810	1258	2630	2959	31	43	63	31
Average of 7 cases after pneumonectomy	3	1916	1793	576	863	2492	2656	23	31	107	67

*Predicted volume of a homologous single normal lung.

†Predicted maximum breathing capacity for a normal subject with intact chest and lungs and of the same age, sex and size.

TABLE IV. (A) INDEX OF INTRAPULMONARY MIXING; (B) VENTILATION AND BREATHING RESERVE AT REST, DURING A ONE-MINUTE STANDARD EXERCISE, AND DURING THE FIRST MINUTE OF RECOVERY IN 7 CASES STUDIED WITHIN A FEW MONTHS AFTER PNEUMONECTOMY (GROUP I)

SUBJECT	TIME AFTER OPERATION (MO.)	INDEX OF INTRAPULMONARY MIXING N_2%	VENTILATION (IN LITERS PER MIN. PER M^2 B.S.)						BREATHING RESERVE (IN LITERS PER MIN.)			
			BASAL		EXERCISE		$RECOVERY_1$		EXERCISE		$RECOVERY_1$	
			PREDICTED	OBSERVED	PREDICTED	OBSERVED	PREDICTED	OBSERVED	PREDICTED	OBSERVED	PREDICTED	OBSERVED
G. H.	1	.82	3.1	4.1	10.0	17.0	13.4	19.8	92	62	80	43
V. Ab.	Before	–	–	–	–	–	–	–	–	–	–	–
	4	2.3	3.1	4.0	10.0	9.7	13.4	9.9	106	23	93	14
A. Am.	Before	1.90	3.6	4.3	–	–	–	–	–	–	–	–
	3	1.21	3.6	5.7	11.0	14.2	12.5	13.9	117	81	107	60
C. Ro.	1½	.73	3.2	4.0	9.0	17.8	10.9	12.1	73	48	66	45
J. Ra.	5	.95	3.6	3.5	11.0	10.8	12.5	10.8	98	67	80	62
C. McL.	5	1.03	3.6	5.4	11.0	12.5	12.5	12.6	84	18	77	22
J. Rut.	Before	1.09	3.9	5.9	11.2	14.5	14.5	21.4	72	63	63	47
	3	1.37	3.9	5.2	11.2	17.9	14.5	22.0	70	43	61	31
Average of 7 cases after pneumonectomy		1.20	3.4	4.6	10.4	14.3	12.8	14.5	91	49	81	39

TABLE V. OXYGEN CONSUMPTION AND ARTERIAL BLOOD OXYGEN SATURATION AT REST, DURING AND FOLLOWING A ONE-MINUTE STANDARD EXERCISE IN 7 CASES STUDIED WITHIN A FEW MONTHS AFTER PNEUMONECTOMY (GROUP I)

SUBJECT	TIME AFTER OPERATION (MO.)	OXYGEN CONSUMPTION IN C.C. PER MIN. PER M^2 B.S.		OXYGEN CONSUMPTION IN C.C. PER LITER OF VENTILATION		ARTERIAL BLOOD OXYGEN SATURATION IN %	
		REST	EXERCISE	REST	EXERCISE	REST	RECOVERY
Normal	11	132	495	44.5	55.4	96.2	95.8
G. H.	1	137	495	40.5	35.1	93.7	95.4
V. Ab.	Before	–	–	–	–	88.0	–
	4	121	416	36.6	51.5	90.6	92.0
A. Am.	Before	150	–	41.8	–	96.9	–
	3	179	566	38.8	49.3	98.8	99.4
C. Ro.	1½	123	540	37.5	36.8	97.2	98.7
J. Ra.	5	140	476	47.1	52.5	98.0	95.0
C. McL.	5	155	471	34.3	44.8	95.3	88.1
J. Rut.	Before	115	544	24.3	45.5	98.0	98.0
	3	114	457	26.3	30.8	99.0	94.0
Average of 7 cases after pneumonectomy	3	138	489	37.3	43.0	96.1	94.7

one to five months after pulmonary resection, and in a few instances control observations before pneumonectomy are available for comparison. The cardiac catheterization technique was used in only 2 cases of this group. In the other cases, therefore, the determination of the effective pulmonary blood flow is based on the assumption that the total pulmonary blood flow was normal and that the oxygen saturation in the mixed venous blood was 25 per cent lower than in the arterial blood. The data will be discussed for the 7 patients considered as a group and then in individual cases.

Average Findings.—Considered as a group and compared with normal standards the 7 subjects studied early after pneumonectomy showed the following findings.

1. In deep inspiration the average size of the remaining lung was slightly greater than that of a normal homologous lung, but the average size in forced expiration was 150 per cent of the predicted size of a normal lung, and the ratio residual air/total capacity × 100 was elevated somewhat above normal.

2. The maximum breathing capacity was reduced to 63 per cent of the predicted value for a normal intact chest with both lungs.

3. A small degree of hyperventilation was present during all the periods of observation. The breathing reserve during the standard exercise test and during the first minute of recovery was respectively 49 and 39 liters, or approximately 45 per cent of the predicted values.

4. The index of intrapulmonary mixing was in the low range of normal, indicating good intrapulmonary distribution of the tidal air and good mixing.

5. The mean oxygen consumption at rest and during the standard one-minute exercise test was normal.

6. The arterial oxygen saturation was approximately normal at rest and very slightly reduced following exercise.

7. The CO_2 tension in the arterial blood while breathing room air was normal at rest and during a steady state of bicycle exercise. The O_2 tension in the

TABLE VI. CO_2 AND O_2 PRESSURE GRADIENTS BETWEEN AMBIENT AIR, ALVEOLAR AIR, AND ARTERIAL BLOOD IN 7 CASES STUDIED WITHIN A FEW MONTHS AFTER PNEUMONECTOMY

SUBJECT	TIME AFTER OPERATION (MO.)	STATE	O_2 TENSIONS (pO_2) (IN MM. HG)			pO_2 GRADIENTS (IN MM. HG)		CO_2 TENSIONS (pCO_2) (IN MM. HG)		TIDAL AIR (IN C.C.)	RESPIRATORY QUOTIENT
			INSPIRED AIR (I)	ALVEOLAR AIR (AL)	ARTERIAL BLOOD (AR)	I-AL	AL-AR	EXPIRED AIR	ARTERIAL BLOOD		
Control Normals		Rest (R. A.)	152	104	94	48	10	26	39	665	.81
		Exer. (B)	151	109	95	42	14	33	38	1064	.90
		Rest (Low O_2)	84	42	33	42	9	23	38	721	.89
G. H.	1	Rest (R. A.)*	151	95	79	56	16	22	42	474	.75
		Rest (Low O_2)	89	58	46	31	12	14	34	538	1.06
V. Ab.	4	Rest (R. A.)	151	96	80	55	16	21	43	387	.79
A. Am.	Before	Rest (R. A.)	153	105	85	48	20	23	36	499	.76
		Exer. (B)	152	105	85	47	20	31	43	1567	.92
	3	Rest (R. A.)	148	97	83	51	14	21	39	820	.77
		Exer. (B)	147	98	82	49	16	23	44	1445	.90
		Rest (Low O_2)	84	49	44	35	5	22	34	864	.98
C. Ro.	1½	Rest (R. A.)*	152	104	100	48	4	22	39	338	.81
		Exer. (B)*	151	118	106	45	12	24	35	558	1.07
		Rest (Low O_2)	71	47	37	24	10	15	31	323	1.28
J. Ra.	5	Rest (R. A.)	153	104	93	49	11	27	39	531	.79
		Rest (Low O_2)	91	47	38	44	9	24	38	586	.87
C. McL.	5	Rest (R. A.)	153	106	84	47	22	19	36	470	.77
		Exer. (B)	152	113	95	39	18	23	35	673	.89
		Rest (Low O_2)	87	49	36	38	13	18	33	450	.88
J. Rut.	Before	Rest (R. A.)	149	103	85	46	18	15	40	485	.87
		Rest (Low O_2)	89	45	40	44	5	15	39	445	.89
	3	Rest (R. A.)	151	113	94	38	19	17	33	370	.86
		Rest (Low O_2)	90	51	44	39	7	15	32	350	.83

*Respiratory gas tensions studied simultaneously with blood flow measurements by cardiac catheterization technique.
Rest (R. A.), Resting state, breathing room air.
Rest (Low O_2), Rest state, breathing a mixture of 12 per cent oxygen in nitrogen.
Exer. (B), Bicycle exercise with steady state.
For averages see Table XII.

TABLE VII. EFFECTIVE ALVEOLAR VENTILATION AND EFFECTIVE PULMONARY BLOOD FLOW IN 7 CASES STUDIED WITHIN A FEW MONTHS AFTER PNEUMONECTOMY

SUBJECT	STATE	ALV. ARTERIAL pO_2 GRADIENT (MM. HG)	PULMONARY BLOOD FLOW: TOTAL (A) (LITERS PER MIN. PER M^2 B.S.)	PULMONARY BLOOD FLOW: EFFECTIVE (B) (LITERS PER MIN. PER M^2 B.S.)	RATIO $\frac{B}{A}$	PULMONARY VENTILATION: TOTAL (C) (LITERS PER MIN. PER M^2 B.S.)	PULMONARY VENTILATION: EFFECTIVE ALV. (D) (LITERS PER MIN. PER M^2 B.S.)	RATIO $\frac{D}{C}$
Normal	Rest	>12	3.10	2.95	>94	3.82	2.97	>70
G. H.	Rest	16	4.68	4.26	91	4.10	2.66	65
V. Ab.	Rest	16	–	–	91.2*	4.08	2.74	67
A. Am.	Rest	14	–	–	92.9*	5.65	3.50	62
C. Ro.	Rest	4	3.21	3.15	98	4.43	3.28	74
	Exercise	12	4.37	4.30	98.5	12.30	9.80	79
J. Ra.	Rest	11	–	–	95.1*	3.54	2.52	71
C. McL.	Rest	22	–	–	92.6*	5.37	3.60	67
J. Rut.	Rest	19	–	–	92.8*	5.21	3.54	68
Average of 7 cases at rest		15	–	–	93.4	4.63	3.12	68
Average of 2 cases at rest in which MVB was sampled		10	4.15	3.56	94.5	4.27	2.97	70

*In cases where the mixed venous blood oxygen saturation was not determined directly, the ratio of effective to total blood flow was calculated assuming a mixed venous blood saturation 25 per cent lower than the determined arterial blood saturation on the basis of the following formula:

$$\frac{\text{Effective blood flow}}{\text{Total blood flow}} \times 100 = \frac{\text{Art. blood } O_2 \text{ sat. \%} - \text{mixed venous blood } O_2 \text{ sat. \%}}{\text{Total capillary } O_2 \text{ sat. \%} - \text{mixed venous blood } O_2 \text{ sat. \%}} \times 100$$

arterial blood during room air breathing was slightly below the accepted normal value and the alveolo-arterial pO_2 gradient was slightly elevated. Using these figures for the calculation of effective pulmonary blood flow and of effective alveolar ventilation expressed in per cent of total blood flow and of total ventilation, it was found that both were slightly below normal standard values, respectively 93.6 and 68 per cent.

8. The average alveolo-arterial pO_2 gradient while breathing a low oxygen mixture was within the normal range in all cases.

9. The total pulmonary blood flow and the pulmonary arterial pressures measured in 2 cases in the resting state were normal.

Comment.—It is apparent from these results that in this group, studied shortly after the resection of one lung, a slight degree of pulmonary distention was present at the time of study. A combination of reduction in maximum breathing capacity and of hyperventilation reduced the breathing reserve to one-half of normal. Readjustments in the distribution of alveolar ventilation and perfusion through the remaining lung were not perfect; compared with a normal lung a slightly greater proportion of alveoli were well perfused but poorly ventilated and also a slightly greater proportion of alveoli were well ventilated but poorly perfused. Finally, there was no evidence of hypertension in the pulmonary circulation at rest, indicating that the vascular bed of the remaining lung was able to accommodate a twofold increase in pulmonary blood flow in a normal manner.

Individual Cases.—Study of the data in the individual cases of this group shows that the physiologic adjustments, apparently influenced by several factors, were quite variable.

1. In two patients, J. Ra. and C. Ro., aged 15 and 22 years respectively, all the data indicate that the remaining lung was in all respects normal (Fig. 2). In both patients resection of the contralateral lung had been performed for bronchial stenosis of tuberculous origin and had been followed by thoracoplasty.

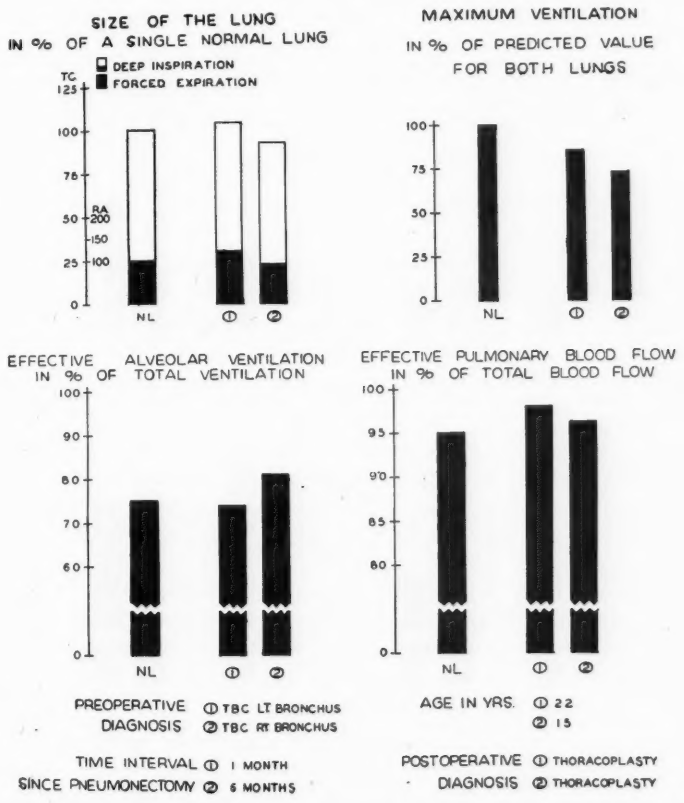

Fig. 2.—Effective alveolar ventilation and pulmonary blood flow in 2 cases with no distention of the lung, studied shortly after pneumonectomy. (*1*) Case C. Ro. and (*2*) Case J. Ra.

After pneumonectomy and thoracoplasty the size of the remaining lung during deep inspiration and forced expiration was entirely comparable with that of a homologous normal lung. The maximum breathing capacity was, respectively, 73 and 85 per cent of the predicted value for both lungs in a normal subject. The breathing reserve during exercise and the first minute of recovery was significantly larger than the average value for the group. The arterial blood oxygen saturation at rest and following exercise was well within normal limits.

The effective pulmonary blood flow at rest was in these two patients, respectively, 98 and 96.1 per cent of the total pulmonary blood flow, and during a steady state of moderate exercise increased to 98.5 per cent of the total flow in the case of C. Ro. (Fig. 8). The effective alveolar ventilation was, respectively, 74 and 81 per cent of the total ventilation. All these figures are well within the normal range.

Pulmonary blood flow and pulmonary arterial blood pressures measured in the case of C. Ro. were also normal at rest.

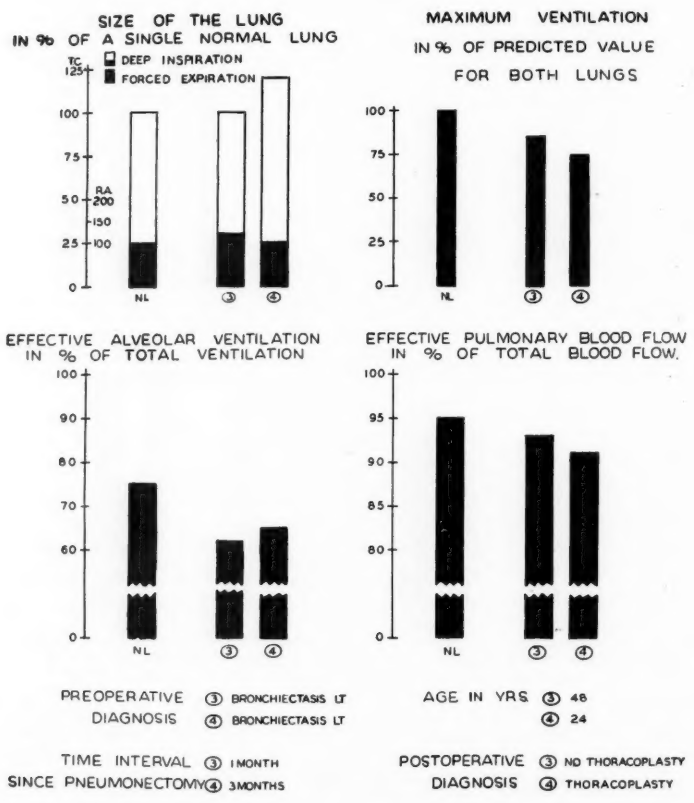

Fig. 3.—Effective alveolar ventilation and pulmonary blood flow in 2 cases with no distention of the lung, studied shortly after pneumonectomy. (3) Case G. H. and (4) Case A. Am.

In summary, the remaining lung in both these cases was not distended and under the conditions of study behaved in an entirely normal manner.

2. In two other patients, A. Am. and G. H., aged 24 and 48 years respectively, the data show that abnormalities in the distribution of alveolar ventilation and perfusion were present (Fig. 3). In these 2 patients the contralateral lung

had been resected for chronic suppuration, associated with organizing pneumonia and fibrosis, and in one case the pneumonectomy was supplemented by thoracoplasty.

Within the next several weeks the remaining lung in both these cases had not become distended, as shown by the measurements of lung volume. The maximum breathing capacity was, respectively, 74 and 84 per cent of the predicted value for two lungs. The breathing reserve was as large during the standard exercise test and the first minute of recovery as in the two previous cases. In one patient the arterial oxygen saturation was slightly below the lower level of normal at rest, and the carbon dioxide tension was normal.

Respiratory gas tension studies, however, indicate that the effective pulmonary blood flow was reduced to, respectively, 92.9 and 91 per cent of total blood flow, and that the effective alveolar ventilation was also reduced to, respectively, 62 and 65 per cent of total ventilation.

The pulmonary blood flow and pulmonary arterial pressure measured in G. H. were normal at rest and during a steady state of moderate exercise, the pulmonary arterial pressure increasing by only 3 mm. Hg.

In summary, there was evidence that the redistribution of alveolar ventilation and perfusion throughout the remaining lung was somewhat impaired. The question is raised, whether in the absence of pulmonary distention these minor changes might not be related to the presence of limited pathologic changes in the remaining lung and were already present before pulmonary resection.

3. In the 3 remaining patients of this group, C. McL., J. Rut., and V. Ab., aged 34, 57, and 35 years, respectively, the data show that the remaining lung was distended or emphysematous and that the alveolar ventilation-perfusion relationships were abnormal (Fig. 4). In these 3 patients the contralateral lung had been resected for a chronic suppurative process associated with organizing pneumonia and fibrosis. In C. McL. and J. Rut. thoracoplasty was performed a short time after pneumonectomy and in both was complicated by a significant degree of scoliosis. In V. Ab. the roentgenograms showed a considerable shift of the mediastinal contents, and the physiologic studies preceded the correction of this shift by thoracoplasty.

Within the next three to five months the remaining lung, as shown by lung volume measurements, was considerably larger than a normal homologous lung in forced expiration, while the size in deep inspiration was lower than normal in one, approximately normal in another, and 150 per cent of normal in the third. Pulmonary distention was therefore present in all 3 cases. The maximum breathing capacity was, respectively, 38, 49, and 31 per cent of the predicted value for both lungs, much lower than in the previous 4 cases. The index of intrapulmonary mixing in V. Ab. was unusually high for a single lung. Hyperventilation was present at rest in the 3 patients and during exercise and recovery in 2 of them; in the third (V. Ab.) relative hypoventilation was observed during these two periods. The arterial oxygen saturation was slightly reduced in all 3 cases, either at rest or following exercise, or in both these states.

Respiratory gas tension studies showed that the calculated effective pulmonary blood flow was, respectively, 92.0, 92.8, and 91.2 per cent of the total blood flow, and that the effective alveolar ventilation was 67, 68, and 67 per cent of the total ventilation.

No observations on the state of the pulmonary circulation are available in any of these cases.

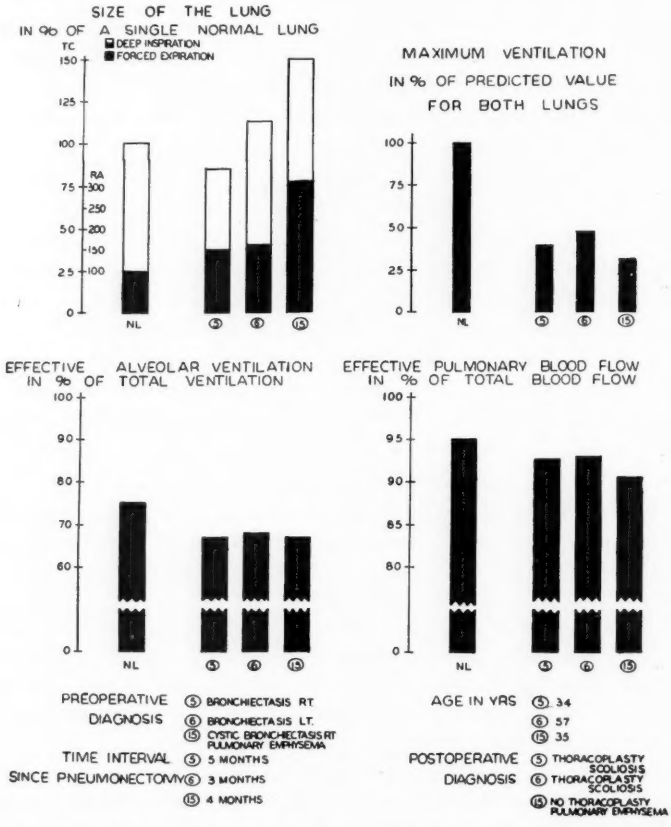

Fig. 4.—Effective alveolar ventilation and pulmonary blood flow in 3 cases with marked distention of the lung, studied shortly after pneumonectomy. (*5*) Case C McL., (*6*) J. Rut. and (*7*) V. Ab.

In summary, the remaining lung in these 3 cases was distended or emphysematous. This condition was accompanied by marked disturbance in the mechanics of the chest bellows, by a considerable reduction in the available breathing reserve, and by some evidence that the distribution of alveolar ventilation and alveolar perfusion was not homogeneous, requiring therefore a large total ventilation to supply adequate alveolar ventilation and causing the arterial blood oxygen saturation to be slightly reduced. The hypothesis that the state of pul-

monary distention might be related to the development of scoliosis, which complicated the thoracoplasties in 2 cases, is supported by the physiologic observations made in one of them before pneumonectomy. The data obtained preoperatively in this case do not suggest the presence of pulmonary distention or emphysema. In contrast, the preoperative studies in the third case, V. Ab., showed that the total capacity was considerably reduced, and that the ratio residual air/total capacity × 100 was very high. Pathologic sections of the resected lung explain in part these findings, as they demonstrated the presence of multiple and large air cysts. The size of the remaining lung postoperatively was markedly increased in both deep inspiration and forced expiration, which finding is explained in part by the marked mediastinal shift observed in roentgenograms and possibly also by the presence of a mild degree of emphysema.

Group II

The data obtained in the 9 patients of this group are tabulated in Tables VIII to XV. Observations were repeated at intervals during several years following resection of one lung. The tables list only the measurements which have not been previously reported. The data on the ventilation-perfusion relationships and on the dynamics of the pulmonary circulation were collected only recently at the time of the latest complete studies listed. In the case of D. M. no such data are available.

Average Findings.—Considered as a group and compared with normal standards the 9 subjects studied late after pneumonectomy showed the following findings.

1. The average size of the remaining lung, in deep inspiration, was 125 per cent of the predicted size of a normal homologous lung in a state of maximum inflation, while its average size in forced expiration was 175 per cent of that of a normal lung in the state of maximum deflation and the ratio residual air/total capacity × 100 was somewhat higher than normal.

2. The maximum breathing capacity was reduced to only 70 per cent of the predicted value for a normal chest with both lungs.

3. A small degree of hyperventilation was present during the three periods of observation at rest, during the standard exercise test, and during the first minute of the recovery period. The breathing reserve during the standard exercise test and the first minute of the recovery period was, respectively, 53 and 47 liters, or approximately 60 per cent of the predicted values.

4. The mean index of intrapulmonary mixing was normal.

5. The mean oxygen consumption at rest and during the standard one-minute exercise test was normal.

6. The mean arterial oxygen saturation was approximately normal at rest and following exercise was slightly below the lower range of normal.

7. The CO_2 tension in the arterial blood, while breathing room air, was normal at rest and during a steady state of bicycle exercise. The oxygen tension was slightly lower than normal in both these states, and the alveolo-arterial pO_2 gradient was at the upper limit of normal. The effective pulmonary blood flow and the effective alveolar ventilation were, respectively, 93.7

TABLE VIII. LUNG VOLUMES AND MAXIMUM BREATHING CAPACITY IN 9 CASES STUDIED SEVERAL YEARS AFTER PNEUMONECTOMY

SUBJECT	TIME AFTER OPERATION (MO.)	VITAL CAPACITY (IN C.C.)		RESIDUAL AIR (IN C.C.)		TOTAL CAPACITY (IN C.C.)		RESIDUAL AIR / TOTAL CAPACITY × 100		MAXIMUM BREATHING CAPACITY (IN LITERS)	
		PREDICTED*	OBSERVED	PREDICTED*	OBSERVED	PREDICTED*	OBSERVED	PREDICTED	OBSERVED	PREDICTED†	OBSERVED
H. W.	131	1820	2910	455	628	2275	3538	20	18	102	86
R. G.	108	2447	3623	611	700	3060	4323	20	16	135	102
S. R.	25	1800	2901	550	819	2350	3720	23	22	124	92
J. Lo.	104	2480	2537	620	1054	3100	3591	20	29	136	76
J. Rus.	1	1485	1912	663	1180	2148	3092	31	38	80	69
	26	1485	1616	663	1374	2148	2990	31	46	80	74
V. Wat.	17	1854	2201	825	976	2679	3147	31	31	89	76
	42	1854	2229	825	1004	2679	3294	31	31	89	65
	50	1854	2154	825	1682	2679	3836	31	44	89	65
	91	1854	2017	825	1590	2679	3607	31	44	79	75
D. M.	13	1990	1930	890	1478	2880	3474	31	43	96	41
	50	1990	1566	890	2247	2880	3985	31	56	96	24
E. Re.	80	2254	2589	687	1139	2941	3728	23	31	104	68
F. I.	15	1733	2396	772	865	2505	3261	31	27	114	73
	77	1733	2342	772	1213	2505	3555	31	34	114	79
Average of 9 cases after pneumonectomy‡	79	1960	2450	685	1163	2644	3630	26	32	108	75

*Predicted volume of a homologous single normal lung.

†Predicted maximum breathing capacity for a normal subject with intact chest and lungs and of the same age, sex, and size.

‡Includes only the latest series of measurements in each case when several studies were made.

TABLE IX. (A) INDEX OF INTRAPULMONARY MIXING; (B) VENTILATION AND BREATHING RESERVE AT REST, DURING A ONE-MINUTE STANDARD EXERCISE AND DURING THE FIRST MINUTE OF RECOVERY IN 9 CASES STUDIED SEVERAL YEARS AFTER PNEUMONECTOMY

SUBJECT	TIME AFTER OPERATION (MO.)	INDEX OF INTRAPULMONARY MIXING (N_2%)	VENTILATION (IN LITERS PER MIN. PER M^2 B.S.)						BREATHING RESERVE (IN LITERS PER MIN.)			
			BASAL		EXERCISE		$RECOVERY_1$		EXERCISE		$RECOVERY_1$	
			PREDICTED	OBSERVED	PREDICTED	OBSERVED	PREDICTED	OBSERVED	PREDICTED	OBSERVED	PREDICTED	OBSERVED
H. W.	131	.89	3.2	3.7	9.0	10.1	10.9	11.4	87	69	79	65
R. G.	108	1.21	3.6	4.0	11.0	14.0	12.5	12.9	115	61	106	80
S. Ro.	25	.91	3.1	4.5	10.0	14.0	13.4	12.1	105	65	92	52
J. Lo.	104	1.37	3.6	3.9	11.0	12.5	12.5	11.9	116	54	104	54
J. Rus.	1	.63	3.9	4.2	11.2	16.3	14.5	20.6	64	45	55	39
	26	.84	3.9	6.2	11.2	22.5	14.5	25.6	64	42	55	29
V. Wat.	17	1.02	3.9	4.3	11.2	11.0	14.5	14.4	69	44	59	50
	42	1.43	–	–	–	–	–	–	–	–	–	–
	50	1.18	3.9	4.4	11.2	16.5	14.5	17.7	68	53	58	32
	91	1.28	3.9	6.3	11.2	17.5	14.5	20.7	61	47	52	31
D. M.	13	1.19	3.9	4.1	11.2	17.4	14.5	16.8	76	30	65	20
	50	2.98	3.9	5.5	11.2	11.6	14.5	13.0	72	3	63	4
E. Re.	80	–	3.1	3.6	10.0	10.3	13.4	10.3	88	75	77	69
F. I.	15	–	3.1	2.5	10.0	12.1	13.4	9.8	96	51	84	49
	79	–	3.9	3.2	11.2	9.6	14.5	11.9	88	61	77	41
Average of 9 Cases*	77	1.35	3.6	4.5	10.6	13.6	13.4	14.4	88	53	78	47

*Includes only the latest series of measurements in each case, when several studies were made.

TABLE X. OXYGEN CONSUMPTION AND ARTERIAL BLOOD OXYGEN SATURATION AT REST, DURING AND FOLLOWING A ONE-MINUTE STANDARD EXERCISE IN 9 CASES STUDIED SEVERAL YEARS AFTER PNEUMONECTOMY

SUBJECT	TIME AFTER OPERATION (MO.)	OXYGEN CONSUMPTION IN C.C. PER MIN. PER M^2 B.S.		OXYGEN CONSUMPTION IN C.C PER LITER OF VENTILATION		ARTERIAL BLOOD OXYGEN SATURATION (IN %)	
		REST	EXERCISE	REST	EXERCISE	BASAL	RECOVERY
Normal		132	495	44.5	55.4	96.0	96.0
H. W.	131	127	476	41.8	56.8	95.0	96.5
R. G.	108	143	519	37.4	45.7	96.2	95.0
S. Ro.	25	146	564	38.8	48.8	95.5	–
J. Lo.	104	132	502	44.6	63.2	97.0	96.0
J. Rus.	1	131	552	36.7	39.4	97.2	97.5
	26	146	586	28.0	31.0	98.0	96.2
V. Wat.	17	116	416	31.0	42.8	93.5	93.6
	42	–	–	–	–	–	–
	50	111	429	29.1	30.4	95.0	97.0
	91	141	427	26.9	29.5	96.0	96.0
D. M.	13	134	512	34.2	34.0	95.6	90.8
	50	126	345	27.0	35.1	91.6	85.4
E. Re.	80	119	548	40.4	64.8	94.4	91.8
F. I.	15	102	442	48.2	42.6	96.6	97.9
	79	119	342	45.2	42.8	95.2	91.0
Average of 9 cases*	77	133	479	36.7	44.2	95.4	93.1

*Includes only the latest series of measurements in each case, when several studies were made.

and 70 per cent of the total blood flow and of the total ventilation in the resting state. In 3 of the cases the measurements repeated during a steady state of moderate exercise showed a significant increase: the effective pulmonary blood flow rose to 97.9 per cent of the total blood flow while the effective alveolar ventilation constituted 79 per cent of the total ventilation.

8. The mean alveolo-arterial pO_2 gradient of the group while breathing a low oxygen mixture was within the normal range.

9. The average pulmonary blood flow and mean pulmonary arterial pressure were within the normal range at rest. During the steady state of moderate exercise the pulmonary arterial pressure rose from 15 mm. Hg at rest to the abnormally high value of 24 mm. Hg.

Comment.—From these results it appears that in this group studied at an average time of seventy-seven months after the resection of one lung, the remaining lung was larger than normal in deep inspiration and was distended in forced expiration. Discussion as to whether the latter finding indicates that a mild degree of chronic pulmonary emphysema was present will be postponed until after presentation of the individual cases.

Compared with the average maximum breathing capacity in the group studied soon after pneumonectomy, the average maximum breathing capacity was reduced less, in spite of a state of greater pulmonary distention, and the breathing reserve was larger during standard exercise and the first minute of recovery. Minor alterations in the distribution of alveolar ventilation and alveolar perfusion were also present. The dynamics of the pulmonary circulation were normal at rest, as in Group I. However, in the course of a moderate exercise the pulmonary arterial pressure became abnormally high. In this state the

TABLE XI. CO_2 AND O_2 PRESSURE GRADIENTS BETWEEN AMBIENT AIR, ALVEOLAR AIR, AND ARTERIAL BLOOD IN 8 CASES STUDIED SEVERAL YEARS AFTER PNEUMONECTOMY

SUBJECT	TIME AFTER OPERATION (MO.)	STATE	O_2 TENSIONS (pO_2) (IN MM. HG)			pO_2 GRADIENTS (IN MM. HG)		CO_2 TENSIONS (pCO_2) (IN MM. HG)		TIDAL AIR (IN C.C.)	RESPIRATION QUOTIENT
			INSPIRED AIR (I)	ALVEOLAR AIR (AL)	ARTERIAL BLOOD (AR)	I-AL	AI-AR	EXP. AIR	ART. BLOOD		
H. W.	131	Rest (R. A.)	151	100	91	51	9	21	36	369	.70
	131	Rest (low O_2)	89	55	43	34	12	20	32	428	.95
	134	Rest* (R. A.)	153	106	94	47	12	19	33	540	.71
	134	Exer.* (L)	152	117	96	35	21	27	33	780	.94
R. G.	108	Rest (R. A.)	148	96	92	50	4	22	42	364	.84
	108	Exer. (B)	148	100	90	48	10	31	43	1120	.90
	110	Rest (low O_2)	82	48	42	34	6	22	38	303	1.11
	110	Rest* (R. A.)	158	107	104	51	3	22	41	332	.81
	110	Exer.* (L)	157	116	110	47	6	29	37	645	.93
S. Ro.	25	Rest (R. A.)	151	109	95	42	14	23	35	506	.83
	25	Exer. (B)	150	112	96	38	16	28	35	1170	.91
	25	Rest (low O_2)	85	49	41	36	8	21	32	570	.93
J. Lo.	104	Rest (R. A.)	150	100	79	50	21	29	46	478	.92
	104	Exer. (B)	151	103	78	48	25	34	40	745	.84
	104	Rest (low O_2)	89	48	41	41	7	27	42	412	1.02
J. Rus.	26	Rest* (R. A.)	153	87	82	66	5	15	46	480	.70
	26	Rest (R. A.)	153	93	88	60	5	16	49	510	.81
	26	Rest (low O_2)	90	54	39	36	15	16	44	598	1.21
V. Wat.	91	Rest (R. A.)	150	97	86	53	11	15	40	390	.75
	91	Exer. (B)	149	111	92	38	19	19	36	929	.95
	91	Rest (low O_2)	101	56	45	45	11	14	35	427	.77
	92	Rest* (R. A.)	150	99	89	51	10	15	41	374	.81
	92	Exer.* (L)	149	104	90	45	14	22	45	653	1.00
E. Re.	81	Rest (R. A.)	152	95	79	57	16	18	46	398	.81
	81	Exer. (B)	153	106	81	47	25	34	39	1040	.83
	81	Rest (low O_2)	86	44	37	42	7	20	43	596	.91
F. I.	79	Rest (R. A.)	151	101	91	50	10	26	40	548	.80
	79	Exer. (B)	151	101	91	50	10	32	42	1230	.84
	79	Rest (low O_2)	85	54	37	31	17	26	32	792	1.03

*Respiratory gas tensions studied simultaneously with blood flow measurements by cardiac catheterization technique.
Rest (R. A.), resting state, breathing room air.
Rest (low O_2), resting state, breathing a mixture of 12 per cent oxygen in nitrogen.
Exer. (B), bicycle exercise with steady state.
Exer. (L), steady state of a leg exercise with subject flat on back.
For averages see Table XII.

TABLE XII. AVERAGE OXYGEN TENSION GRADIENTS BETWEEN INSPIRED AIR, ALVEOLAR AIR, AND ARTERIAL BLOOD AND AVERAGE ARTERIAL CARBON DIOXIDE TENSIONS IN TWO GROUPS OF SUBJECTS AFTER PNEUMONECTOMY

STATE	GROUP	NO. OF CASES	O_2 TENSIONS (pO_2) (IN MM. HG)			pO_2 GRADIENTS (IN MM. HG)		CO_2 TENSIONS (pCO_2) (IN MM. HG)
			INSPIRED AIR (I)	ALVEOLAR AIR (AL)	ARTERIAL BLOOD (AR)	I-AL	AL-AR	ARTERIAL BLOOD
Rest, R. A. breathing	Normal	8	152	104	94	48	10	39
	Group I	7	151	102	87	49	15	39
	Group II	8	152	100	89	52	12	41
Rest, low O_2 breathing	Normal*	3	84*	42*	33*	42*	9*	38*
	Group I	6	85	50	41	35	9	34
	Group II	8	88	51	41	37	10	37
Exercise, bicycle, steady state	Normal	8	151	109	95	42	14	38
	Group I	3	150	110	94	40	16	38
	Group II	6	150	106	88	44	18	39

*Arterial blood CO_2 and oxygen tension measurements with low oxygen breathing made in only 3 of the 8 normal physicians recently studied. In a much larger control group previously studied by Lilienthal and associates[6] similar values were obtained.

TABLE XIII. EFFECTIVE ALVEOLAR VENTILATION AND EFFECTIVE PULMONARY BLOOD FLOW IN 7 CASES STUDIED SEVERAL YEARS AFTER PNEUMONECTOMY

SUBJECT	STATE	ALV. ARTERIAL pO_2 GRADIENT (MM. HG)	PULMONARY BLOOD FLOW		RATIO B/A	PULMONARY VENTILATION		RATIO D/C
			TOTAL (A) (LITERS PER MIN. PER M^2 B.S.)	EFFECTIVE (B) (LITERS PER MIN. PER M^2 B.S.)		TOTAL (C) (LITERS PER MIN. PER M^2 B.S.)	EFFECTIVE ALV. (D) (LITERS PER MIN. PER M^2 B.S.)	
Normal	Rest	<12	3.10	2.95	>95.0	3.82	2.97	>70
H. W.	Rest	12	3.44	3.29	95.4	4.26	2.94	69
	Exercise	21	5.15	5.00	97.1	9.48	8.75	91
R. G.	Rest	3	3.17	3.11	98.0	4.04	2.99	74
	Exercise	6	6.24	6.19	99.1	12.40	10.90	88
S. Ro.	Rest	14	–	–	94.7*	4.53	3.81	79
J. Lo.	Rest	21	2.94	2.67	90.6	3.86	3.01	78
J. Ru.	Rest	5	3.15	3.05	95.0	6.08	3.70	61
V. Wat.	Rest	10	2.29	2.21	96.7	5.63	2.98	53
	Exercise	14	3.24	3.13	97.6	10.76	6.25	58
E. Re.	Rest	16	3.52	3.05	86.8	3.41	2.52	74
F. I.	Rest	10	2.94	2.74	93.2	3.15	2.42	77
Average of 8 cases at rest		11	3.06	2.87	93.7	4.36	3.05	70
Average of 3 cases during exercise		14	4.88	4.77	97.9	10.88	8.63	79

*Mixed venous blood not collected. Mixed venous blood O_2 saturation per cent assumed to be 25 per cent lower than arterial blood saturation.

TABLE XIV. EFFECTIVE ALVEOLAR VENTILATION AT REST AND DURING THE STEADY STATE OF A BICYCLE EXERCISE IN A GROUP OF 8 CASES AFTER PNEUMONECTOMY

STATE	GROUP	NO. OF CASES	$\frac{\text{ALV. VENTILATION}}{\text{TOTAL VENTILATION}} \times 100$	ALV. VENTILATION (LITERS PER MIN. PER M^2 B.S.)	O_2 INTAKE (C.C. PER MIN. PER M^2 B.S.)	O_2 INTAKE (C.C. PER LIT.) ALV. VENTILATION
Rest	Normal	8	78	2.97	141	48
	Pneumonectomy Groups I*-II	8	71	3.16	145	46
Exercise, steady state	Normal	8	88	12.80	567	44
	Pneumonectomy Groups I*-II	8	75	10.95	523	48

*This mixed group includes the cases A. Am. and C. McL. from Group I and all the cases from Group II except H. W.

pulmonary blood flow through the remaining lung was larger than the blood flow through each lung of a normal individual performing a very severe type of exercise. Under such circumstances the pulmonary arterial pressure of the normal individual remains normal.[7, 8] The various mechanisms involved in the abnormal increase of the pulmonary arterial pressure will be discussed later.

Individual Cases.—Examination of the data in the individual cases of this group reveals marked variations in their physiologic status.

1. In 3 patients, S. R., H. W., and R. G., aged 41, 17, and 21 years, respectively, the data indicate that the remaining lung was normal as far as can be judged from the studies (Fig. 5). Two of the cases, H. W., and R. G., have already been discussed in two previous reports.[1, 2] The data concerning the alveolar ventilation-perfusion relationships and the dynamics of the circulation obtained recently confirm and supplement the general impression reached on the basis of the previously reported less complete studies of pulmonary function. In these 3 patients the resection had been performed for chronic suppuration of one lung and had not been followed by thoracoplasty.

It is quite remarkable that the size of the lung in these 3 subjects at the end of the deepest inspiration was approximately 150 per cent of that of a normal homologous lung in the same respiratory position. This finding was obviously due to a mediastinal shift which is well known to occur during deep inspiration. However, in forced expiration the size of the deflated lung was about that of a normal homologous lung, as shown by the ratio residual air/total capacity $\times$ 100, which was, respectively, 22, 18, and 16. The maximum breathing capacity was, respectively, 74, 84, and 76 per cent of the predicted value for both lungs and the breathing reserve in the absence of any significant degree of hyperventilation during the standard exercise test and the first minute of recovery was very large, ranging from 60 to 80 per cent of predicted normal values. The arterial oxygen saturation at rest and during exercise was within the normal range of variation in all 3 cases.

Studies of the ventilation-perfusion relationships in these 3 subjects demonstrated that the effective pulmonary blood flow was, respectively, 94.7, 95.4, and 97 per cent of the total pulmonary blood flow and that the effective alveolar

TABLE XV. PULMONARY BLOOD FLOW AND PULMONARY ARTERIAL PRESSURES AT REST AND DURING THE STEADY STATE OF A MODERATE EXERCISE* IN 9 CASES AFTER PNEUMONECTOMY

SUBJECT	TIME AFTER OPERATION (MO.)	STATE	PULSE RATE	O_2 CONSUMPTION (C.C. PER MIN. PER M^2 B.S.)	ARTERIAL VENOUS O_2 DIFFERENCE (C.C. PER LITERS)	CARDIAC OUTPUT		ARTERIAL BLOOD PRESSURES				SYSTEMIC VASCULAR RESISTANCE DYNES CM.$^{-5}$ SEC. / M^2 B.S.
						LITERS PER MIN. PER M^2 B.S.	S.V.	PULMONARY		SYSTEMIC		
								S/D (MM. HG)	MEAN (MM. HG)	S/D (MM. HG)	MEAN (MM. HG)	
Normal		Rest†		126	39	3.27	83	20/9	13	112/65	84	2090
(average of 3)		Exer. (B)†		406	73	5.40	104	23/4	11	125/78	100	1515
G. H.	1	Rest	113	145	31	4.68	74	25/6	14	130/72	93	1980
		Exer. (L)	132	268	47	5.57	76	35/8	17	160/86	109	1960
C. Ro.	1½	Rest	96	135	42	3.21	47	24/9	14	127/85	102	2550
		Exer. (B)	133	315	72	4.37	52	–	–	145/95	114	2090
H. W.	134	Rest	73	127	37	3.44	89	18/9	12	114/65	81	2500
		Exer. (L)	108	319	62	5.15	85	23/14	17	142/82	98	2000
R. G.	110	Rest	65	127	40	3.17	81	23/7	12	116/71	89	2240
		Exer. (L)	105	443	71	6.24	105	35/19	24	152/84	110	1410
J. Lo.	104	Rest	70	165	56	2.94	77	27/–	–	130/81	94	2560
J. Ru.	26	Rest	101	144	46	3.15	45	36/8	19	115/68	89	2260
V. Wat.	92	Rest	98	119	52	2.29	39	30/13	19	151/91	111	3880
		Exer. (L)	108	259	80	3.24	50	44/24	31	195/113	140	3460
E. Re.	81	Rest	61	123	35	3.52	95	24/7	12	117/62	89	2020
		Exer. (L)	102	277	55	5.04	80	34/11	18	125/68	95	1510
F. I.	79	Rest	59	112	38	2.94	94	29/11	16	143/69	101	2750
		Exer. (L)	97	196	56	3.50	68	55/17	28	171/96	128	2930
Average of 9 cases at rest			82	133	42	3.27	71	26/9	15	127/74	95	2526
Average of 7 cases at rest			81	127	39	3.32	74	25/9	14	128/74	95	2560
Average of 7 cases during exercise			112	297	63	4.74	74	38/16	23	155/89	113	2193

*Measurements started after 10 minutes of a moderate leg exercise with subject flat on back, except in Case C. Ro. where the measurements were started during the tenth minute of a moderate bicycle exercise.

†Data obtained on 3 normal physicians.[8]

ventilation was, respectively, 79, 74, and 69 per cent of the total ventilation. All these figures are normal. Observations made during a steady state of moderate exercise in 2 of the subjects (Fig. 8) showed a marked increase in the efficiency of alveolar perfusion and ventilation. The pulmonary membrane diffusion gradient was normal.

The pulmonary blood flow and the pulmonary arterial blood pressure measured in H. W. and R. G. were normal at rest. In the course of moderate exercise during which the pulmonary blood flow was nearly twice the resting blood flow and significantly larger than the volume of blood flowing through each lung of a normal individual during a severe type of exercise, the mean pressure rose from 12 mm. Hg at rest to 17 and 24 mm. Hg, respectively.

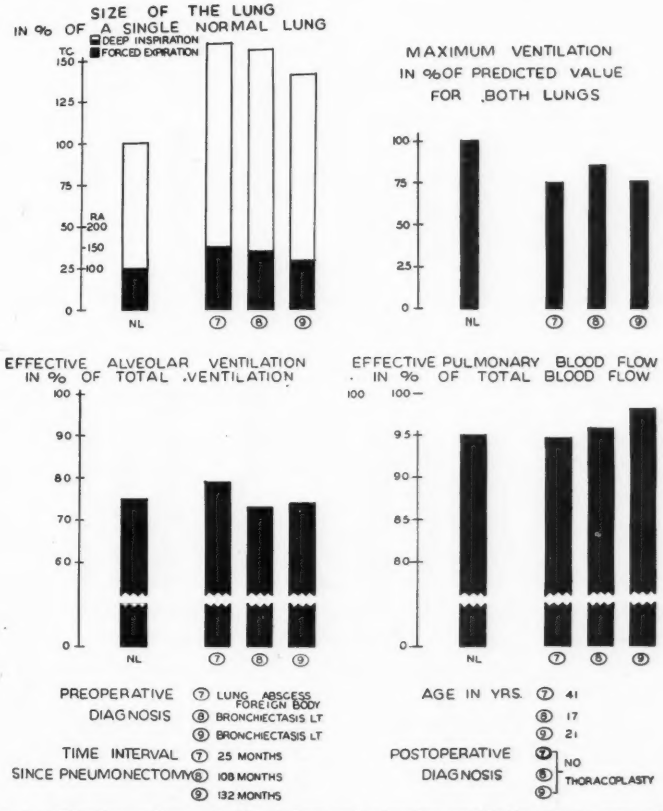

Fig. 5.—Effective pulmonary blood flow and alveolar ventilation in 3 cases with no lung distention, studied several years after pneumonectomy. (7) Case S. Ro., (8) Case H. W., and (9) Case R. G.

In summary, the remaining lung in these 3 cases, although larger than normal in the state of maximum inflation, functioned normally. The physical activity of these 3 subjects was not limited, the reduction in breathing capacity

was slight, and a study of the relationships between alveolar ventilation and alveolar perfusion revealed these to be entirely normal at rest as well as during moderate exercise. This latter finding is of interest since during this exercise the total ventilation and total pulmonary blood flow through the remaining lung reached greater values than those hitherto observed through each lung of normal individuals during a severe exercise test. The only abnormal finding was the observation of a mild degree of pulmonary hypertension during the performance of the exercise. The meaning of this observation will be considered later in the discussion.

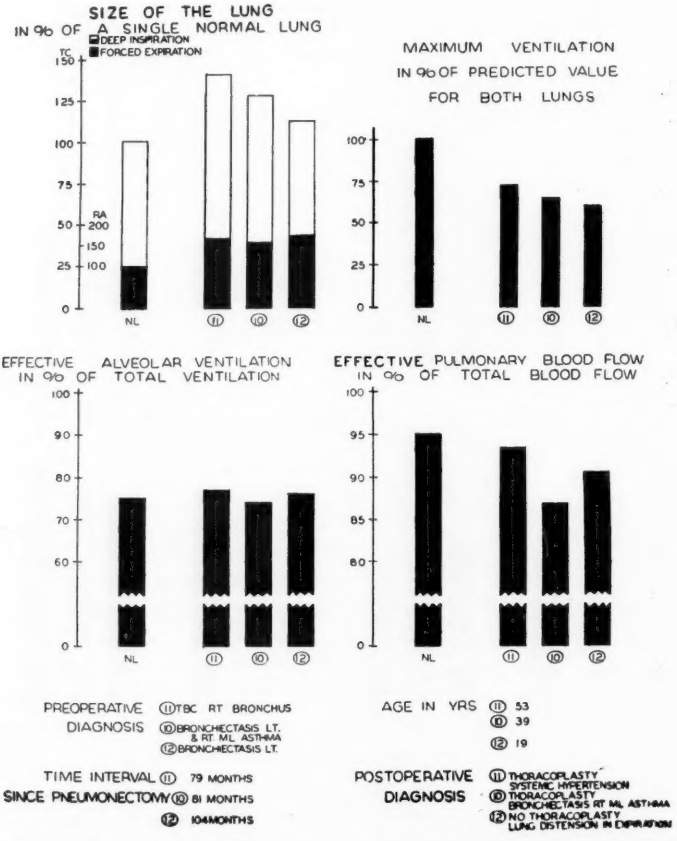

Fig. 6.—Effective pulmonary blood flow and alveolar ventilation in 3 cases with moderate lung distention, studied several years after pneumonectomy. (*10*) Case E. Re., (*11*) Case F. I., and (*12*) Case J. Lo.

2. In 3 patients, F. I., E. Re., and J. Lo., aged 53, 39, and 19 years, respectively, the data show a small degree of pulmonary distention associated with slight abnormalities in the distribution of alveolar ventilation and alveolar perfusion in the remaining lung (Fig. 6). All of these cases have already been dis-

cussed in 3 previous reports[1, 2, 3] on the basis of less complete data. The resection of the lungs in E. Re. and J. Lo. had been performed for chronic suppuration of one lung; in addition E. Re. showed, and still shows, evidence of bronchiectasis in the middle lobe of the remaining right lung, and is suffering from persistent but mild asthma. In F. I. the resection of the right lung was done for stenosis of the right main bronchus of tuberculous origin, which caused over a period of twenty years acute and repeated episodes of bronchial obstruction. In E. Re. and F. I. the pneumonectomy was followed by thoracoplasty.

In these 3 subjects the size of the remaining lung compared with that of a normal homologous lung in the same state was increased in deep inspiration, more so in F. I., less so in J. Lo. In contrast to the 3 previous cases, however, the size of the lung in forced expiration is significantly greater than that of a normal lung in the same state, the state of moderate distention being the greatest in J. Lo., the least in F. I. The maximum breathing capacity was in 2 of the 3 cases reduced more than in the 3 previous cases. Its values in F. I., E. Re., and J. Lo., respectively, 73, 65, and 56 per cent of the predicted normal value with both lungs, bearing a striking relationship to the degree of distention. Hyperventilation did not develop in any of these cases during or following exercise and the moderate reduction of breathing reserve during the standard exercise test and the first minute of recovery was related to the reduction in maximum breathing capacity. Measurements of the arterial oxygen saturation in F. I. and E. Re. at rest and following exercise were somewhat lower than normal, especially after exercise, suggesting that some poorly ventilated alveoli were still perfused.

More precise methods of studies of the ventilation-perfusion relationships demonstrated that at rest the effective pulmonary blood flow was in F. I., E. Re., and J. Lo., respectively, 93.2, 86.8, and 90.6 per cent of the total pulmonary blood flow. In contrast to these figures, which indicate perfusion of poorly or nonventilated alveoli in varying degree, the effective alveolar ventilation was, respectively, 77, 76, and 78 per cent of total ventilation. These figures indicate that there was no ventilation of poorly perfused areas. The pulmonary membrane diffusion gradient was normal in two of the subjects and slightly elevated in F. I.

The pulmonary blood flow and pulmonary blood pressure were normal at rest in the 3 cases. During moderate exercise the pulmonary arterial pressure rose in E. Re. from 12 to 18 mm. Hg when the pulmonary blood flow was 144 per cent of the resting blood flow, and in F. I. it rose from 16 to 28 mm. Hg when the pulmonary blood flow was only 119 per cent of the resting flow. It should be noted (Table XV) that in the case of F. I. the systemic arterial pressure rose considerably during a steady state of very moderate exercise and that the calculation of the systemic vascular resistance indicated some degree of vasoconstriction rather than the usual vasodilatation observed during exercise. The question is raised, therefore, whether a latent state of systemic hypertension was not revealed during the increased physical activity. The development of pulmonary hypertension, if this assumption is correct, would be the result of an increase in pressure in the pulmonary venous bed due to poorer emptying of the

left ventricle in the face of an increasing peripheral resistance rather than the result of an increased resistance through a pulmonary vascular bed restricted in its distensibility.

In summary, the remaining lung in these 3 cases was not normal. A combination of pulmonary distention and of pathologic changes certainly related in one case, probably related in the 2 other cases, to the chronic process for which the controlateral lung was resected, resulted in the persistence of pulmonary flow through areas of the lung which were not ventilated. In the greater part of the lung, however, the relationship between alveolar ventilation and perfusion was normal. It is of importance to note that observations over a long period of years have not shown any significant change in the degree of pulmonary distention in these 3 cases. This state of distention probably was present shortly after pneumonectomy and might be due partly to an underlying pathologic process. It may have been somewhat accentuated following the resection, but at all events was limited by the fixation of the mediastinum in its normal position with or without the help of thoracoplasty.

3. In the 3 remaining cases, D. M., J. Ru., and V. Wat., aged, respectively, 66, 61, and 72 years, the data show that the remaining lung was the site of chronic pulmonary emphysema of mild to moderate degree. In these 3 cases the lung had been resected for carcinoma of a main bronchus and pneumonectomy was not supplemented by thoracoplasty. The survival times up to the last observations were, respectively, fifty, twenty-six, and ninety-one months. One of these 3 patients (D. M.) died after a seventy-two month survival, following an acute respiratory infection.

Physiologic studies of patient D. M. have been reported previously.[3] The preoperative studies showed a marked degree of chronic bilateral pulmonary emphysema of the obstructive type. Postoperative studies fifty months after pneumonectomy indicated that the state of chronic obstructive emphysema had become more severe. The ratio residual air/total capacity $\times$ 100 rose from 43 to 56, the maximum breathing capacity decreased from 41 to 24 liters. The breathing reserve during the standard exercise test and the first minute of recovery was negligible and consequently dyspnea was severe and prolonged. The arterial oxygen saturation was reduced to 91.6 per cent at rest and decreased to 85.4 per cent following the standard exercise test. This finding suggests considerable perfusion of poorly ventilated or nonventilated alveoli. The last physiologic studies, performed three years ago, do not include observations on gas tensions performed simultaneously with cardiac catheterization. Hence a quantitative study of the abnormalities in the distribution of alveolar ventilation and perfusion is not available.

In the other 2 cases, J. Ru. and V. Wat., repeated measurements of lung volume have demonstrated the slow development of a moderate type of nonobstructive emphysema which was not present shortly, or even several months, after pneumonectomy (Fig. 7). The size of the remaining lung on deep inspiration was at the time of the last studies 139 and 135 per cent, respectively, of the predicted size of a normal homologous lung in the same state. In forced expiration the size of the lung was 208 and 193 per cent, respectively, of the

predicted size of a normal homologous lung in the same state. Clinical studies and examination of the spirograms[8] did not reveal any evidence of bronchiolar obstruction. A remarkable finding was that the maximum breathing capacity in these 2 patients was, respectively, 93 and 95 per cent of the predicted values with both lungs. In absolute terms, the maximum breathing capacity was as large as in the 3 previous subjects who were younger and showed a far lesser degree of pulmonary distention in expiration. Marked hyperventilation was

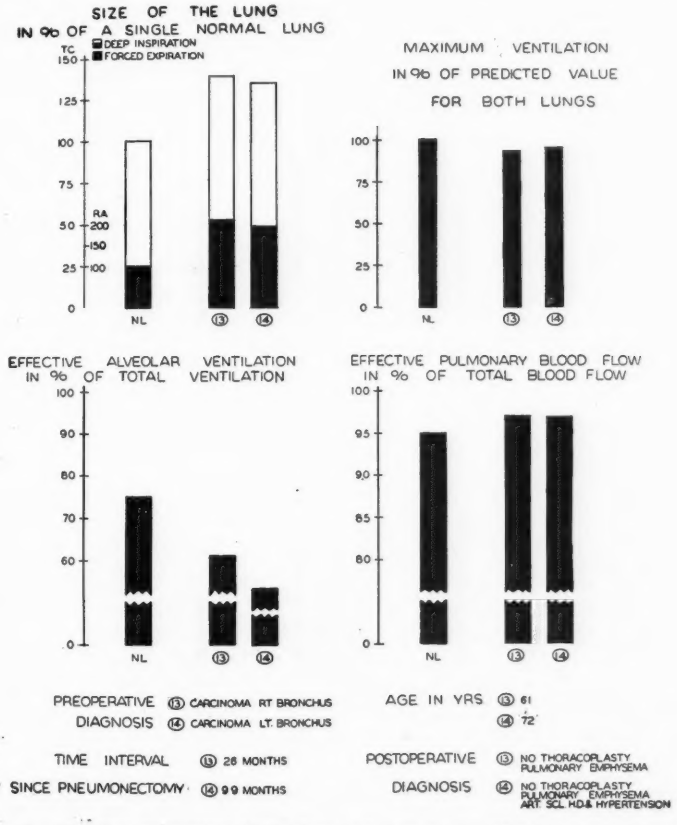

Fig. 7.—Effective pulmonary blood flow and alveolar ventilation in 2 cases of elderly subjects with mild nonobstructive emphysema, studied several years after pneumonectomy. (*13*) Case J. Rus. and (*14*) Case V. Wat.

present during the 3 periods of observation. Consequently, the breathing reserve was reduced below normal values. It was approximately 55 per cent of normal during the first minute of recovery following the standard exercise test and mild dyspnea of short duration was present at that time. The index of intrapulmonary mixing was normal. The arterial blood saturation at rest and following the standard exercise test was well within the normal range of variation.

The respiratory gas tension studies demonstrated that at rest the effective pulmonary blood flow was, respectively, 96.7 and 97 per cent of the total pulmonary blood flow. During a steady state of moderate exercise the effective blood flow rose in one patient, V. Wat., to 97.6 per cent of the total blood flow (Fig. 8). These figures indicate that virtually all perfused areas were well ventilated. These gas tension studies revealed, however, that a large proportion of well ventilated alveoli were poorly perfused or nonperfused. The effective alveolar ventilation in per cent of total ventilation reached the lowest figures in the entire group of patients after pneumonectomy, respectively, 61 and 53 per cent. In V. Wat. during the steady state of moderate exercise the effective

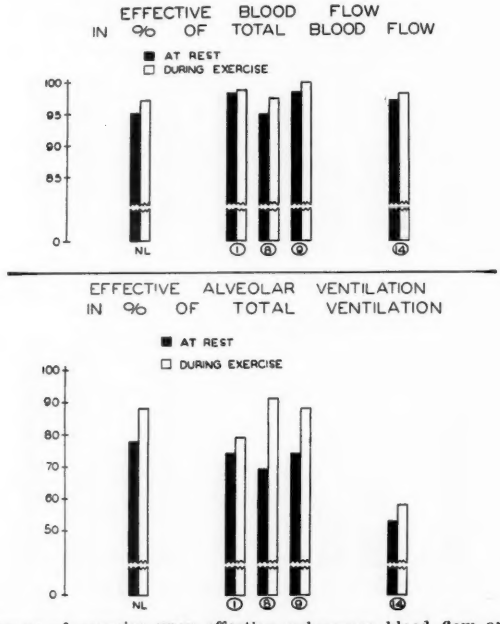

Fig. 8.—Influence of exercise upon effective pulmonary blood flow and alveolar ventilation in 3 young adults with no distention of the lung and in an elderly subject with nonobstructive pulmonary emphysema. (*1*) Case C. Ro., (*8*) Case H. W., (*9*) Case R. G., and (*14*) Case V. Wat.

alveolar ventilation was still only 58 per cent of the total ventilation (Fig. 9). On the basis of these figures it would appear that the pulmonary vascular bed was restricted in parts of the lung which were still effectively ventilated, although whenever alveolar perfusion persisted the alveoli were well ventilated. The pulmonary membrane diffusion gradient was normal in V. Wat. and very slightly elevated in J. Ru.

Studies of the dynamics of the pulmonary circulation showed definite abnormal features. In J. Ru. with an apparently normal cardiovascular system the pulmonary blood flow was normal at rest, but the pulmonary arterial pressure was elevated to 19 mm. Hg. This elevation of mean pulmonary arterial

pressure at a level of blood flow through one lung which normally does not cause any pressure elevation suggests a limitation in the expansibility of the vascular bed. Reduction in the number of small vessels and/or a decrease in the cross-section of the lumen of the arterioles and precapillaries are the most likely causes

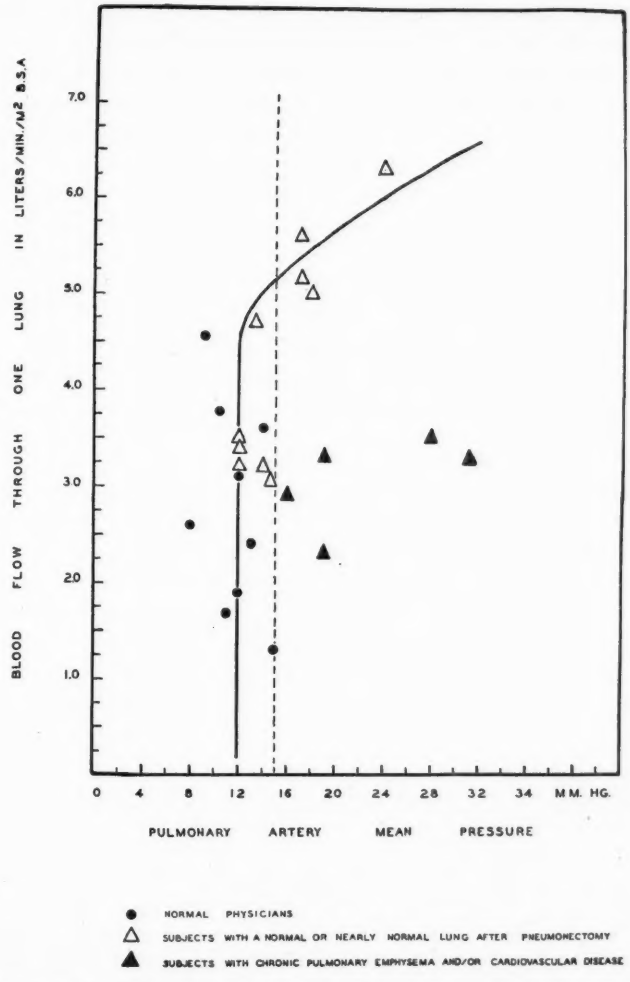

Fig. 9.—Relationship between blood flow through one lung and mean pulmonary arterial pressure in 3 normal subjects and 8 subjects after pneumonectomy.

of this limitation. Since it was demonstrated by the gas tension technique that the blood flow was suppressed in fairly large areas of the lung this finding may be related to the elevated pulmonary artery pressure. In V. Wat., studies of the pulmonary blood flow and pulmonary arterial pressure were made also at

rest and repeated during a steady state of moderate exercise. The pulmonary blood flow at rest was low, and the pulmonary arterial pressure was abnormally elevated to 19 mm. Hg at a level of blood flow through one lung which in normal subjects does not increase pulmonary arterial pressure. During a steady state of moderate exercise the mean pressure in the pulmonary artery rose to the high value of 31 mm. Hg, while the pulmonary blood flow increased to 142 per cent of the resting blood flow. The interpretation of the data is somewhat complicated by the presence in this case of generalized systemic arteriosclerosis associated with systemic hypertension. There is evidence to support the view that the cardiac output is sometimes reduced in systemic hypertension, although clinical and physiologic manifestations of pulmonary venous hypertension may not be present.[12] However, in V. Wat. the exercise tolerance was remarkable and the cardiac output increase during moderate exercise was fairly large, a finding which does not favor the diagnosis of incipient left ventricular insufficiency. Therefore, the possibility of a restriction to the pulmonary vascular bed as a cause of pulmonary hypertension may well be considered also in this case.

In summary, the remaining lung in these 2 cases was the site of chronic emphysematous change of a nonobstructive type. This process originated some time after pneumonectomy, causing alterations in the distribution of alveolar ventilation and perfusion of an unusual character. The pattern of alteration was distinct from that observed in a third patient in whom pneumonectomy was performed in the presence of chronic pulmonary emphysema of the obstructive type. In this case the studies of respiratory gas tensions were not made, but the reduction of the arterial blood oxygen saturation at rest and during the standard exercise test indicates that poorly ventilated alveoli were still perfused. As a result of restriction of the vascular bed in areas of the lung still effectively ventilated, the total ventilation in J. Ru. and V. Wat. was almost double that of normal in all states of physical activity. Whether this constant state of hyperventilation contributed to the maintenance of a large breathing capacity in the presence of a moderate degree of nonobstructive emphysema is a matter of interesting speculation, and is in agreement with similar observations made in an entirely different group of subjects with chronic pulmonary disease.[13] The study of the dynamics of the pulmonary circulation which revealed a state of mild pulmonary hypertension at rest, more severe in one case during exercise, suggests that the pulmonary vascular bed was limited in its distensibility or restricted in its size. An alternate and/or complementary explanation is offered that in the case with generalized arteriosclerosis and systemic hypertension a latent state of left ventricular insufficiency existed. This would cause an increase in pulmonary venous pressure of which the pulmonary artery pressure would be a reflection.

DISCUSSION

The data presented in this paper will be discussed from 3 different points of view, as they may interest the physiologist, the pathologist, and the chest surgeon.

1. In previous papers dealing with the subject of physiologic readjustments after pneumonectomy several conclusions had been reached. These are well supported by some observations reported here.

(a) The size of the lung in deep inspiration is greater than that of an homologous normal lung, since mediastinal displacement toward the contralateral side is not prevented in the state of maximum inflation by the presence of a contralateral lung.

(b) The reduction of maximum breathing capacity is much less than expected from the volumetric reduction of the chest bellows, unless a significant degree of pulmonary distention develops. Good coordination in the functioning muscles of the chest cage and the absence of any obstruction to air flow help to maintain the efficient utilization of the remaining ventilatory space.

(c) The increase of the ratio effective tidal air/functional residual air, which takes place whenever the total ventilation is performed by a single lung, improves the intrapulmonary mixing of gas.

The quantitative relationships existing between alveolar ventilation and alveolar perfusion in a single lung, early and late, after pneumonectomy have also been studied. It would appear from these studies that in children, young adults, or middle-aged subjects, the adjustments are nearly perfect as long as the remaining lung is free of persisting pathologic change or does not become unduly distended as a result of mediastinal dislocation. However, if such changes are present two types of abnormalities in the distribution of ventilation and blood flow are observed, both characterized by a reduction in the percentage of effective blood flow (perfusion of poorly ventilated alveoli) but associated in the first type only with a reduction in the percentage of alveolar ventilation (ventilation of poorly perfused alveoli). These abnormalities are always slight and related to pulmonary distention and/or discrete pathologic processes. In 2 elderly patients with manifestation of mild nonobstructive emphysema a third type of abnormality was observed, characterized by a reduction in the percentage of the effective alveolar ventilation (ventilation of poorly perfused alveoli), while the percentage of effective pulmonary blood flow (perfusion of well-ventilated alveoli) remained normal. This abnormality is different from that which is observed in patients with bilateral obstructive emphysema where very low effective pulmonary flow and effective alveolar ventilation are found.[14] It suggests a pathologic process restricting the vascular bed alone and creating thereby a need for a considerable increase in total ventilation in order to maintain normal gas exchanges through effective alveolar ventilation of well-perfused pulmonary capillaries. As a result, the breathing reserve is reduced in all states of physical activity with a resultant greater tendency to dyspnea.

Studies of the diffusion of oxygen across the pulmonary membrane indicate that it takes place in a normal manner. If it is postulated that in pneumonectomy the potential number of capillaries is reduced by one-half, the persistence of a normal alveolo-arterial pO_2 gradient at a low level of oxygenation means that the area available for diffusion at rest is nonetheless adequate. The number

of capillaries perfused at rest, therefore, compares favorably with the number of capillaries perfused in both lungs of normal subjects under the same basal conditions. Any pathologic process which encroaches upon the vascular bed of the remaining lung should tend to increase this gradient and, therefore, should tend to decrease the diffusion constant of the lung, defined as the amount of oxygen in cubic centimeters which will diffuse from the alveoli into the blood per minute in response to a mean pressure gradient of 1 mm. Hg.[15] This diffusion constant of the lung, which varies according to the size of the diffusing area, has been calculated in 5 cases, using the graphic method developed by Lilienthal and associates.[6] Other cases in this series in which the oxygen consumption was too high for useful comparison have been excluded. As seen in Table XVI, the diffusion constant in 3 young subjects with pneumonectomy was remarkably close to the average figure obtained in a group of young adults with two lungs.[6] In the older subjects, G. H. and V. Wat., aged, respectively, 48 and 72 years, the figures are somewhat lower. In the absence of comparable figures in a group of normal subjects of the same age, it cannot be stated whether or not they are abnormally low. However, they suggest a reduction in the size of the diffusing surface, that is, a reduction in the number of capillaries, which in the case of V. Wat. is consistent with the results of the study of ventilation-perfusion relationships discussed previously.

TABLE XVI. APPROXIMATE DIFFUSION CONSTANT OF THE LUNG IN 5 CASES AFTER PNEUMONECTOMY

SUBJECT	AGE (YR.)	O_2 CONSUMPTION		TIDAL AIR		ALV.-ART. pO_2 GRADIENT		MEMBRANE COMPONENT	MEAN ALV.-CAP. pO_2 GRADIENT	DIFFUSION CONSTANT* $D\,O_2$
		HIGH (C.C. PER MIN.)	LOW (C.C. PER MIN.)	HIGH (C.C.)	LOW (C.C.)	HIGH (MM. HG)	LOW (MM. HG)	LOW (M) (MM. HG)	ΔpO_2 (MM. HG)	
Normal (average of 6) †	33	–	258	–	–	9	9.5	8.9	13.3	21
J. Ra.	15	222	234	531	586	11	9	8.2	12	20
J. Lo.	19	254	245	478	412	21	7	5.6	10	25
R. G.	21	254	246	364	303	4	6	5.7	10	25
G. H.	48	247	223	424	474	16	12	10.9	16	14
V. Wat.	72	228	234	390	427	11	11	10.2	15	16

*Calculated from Fig. 5 (in Lilienthal et al.[6])
†From data collected by Lilienthal et al.[6]; ages ranged from 28 to 36 years.

The observations of the dynamics of the pulmonary circulation provide an unusual opportunity for the study of the deformability of the pulmonary vascular bed at a rate of blood flow through one lung exceeding that observed so far in normal subjects. In studies reported recently[8] on 3 normal subjects, the mean pulmonary arterial pressure was found not to change as the pulmonary blood flow increased up to nearly 10 liters per minute per m^2 B.S. during a steady state of severe exercise. The calculated pulmonary vascular resistance was reduced at that level of blood flow to one-third of its value in the resting state. Similar observations have been made independently by Hickam and Cargill.[7]

In Fig. 9 the blood flow through each lung of these normal individuals at various levels of activity is plotted against the mean pulmonary arterial pressure. It is seen that the mean pulmonary arterial pressure remained less than 15 mm. Hg with blood flow through each lung up to 5 liters per minute per m^2 B.S. With a pulmonary blood flow of less than 5 liters per minute per m^2 B.S. the mean pulmonary arterial pressure remained within normal limits in 5 observations made in 5 subjects after pneumonectomy. In 4 of them during moderate exercise, the mean pulmonary arterial pressure rose progressively as the blood flow increased beyond this level. As all these subjects had a normal or nearly normal lung, they revealed a fundamental characteristic of the curve relating blood flow to pressure in the pulmonary vascular bed by reaching a rate of blood flow through one lung exceeding that observed in normal individuals. The distensibility curve of the pulmonary vascular bed, which is straight and vertical up to a blood flow of 5 liters per minute per m^2 B.S. shows a definite inflection at this level. The characteristics of this curve are of potential interest in the interpretation of the possible causes of pulmonary hypertension in congenital defects of the heart and of the large vessels. If the same curve applies to very young children as well as to adults, it would seem that a moderate increase in the mean pulmonary arterial pressure, with a blood flow of less than 5 liters per minute per m^2 B.S. through each lung is due either to pulmonary vascular changes or to pulmonary venous hypertension. Above this level of flow, an additional factor must be considered, as a large blood flow by itself may cause pulmonary hypertension.

In the remaining 5 observations, plotted in Fig. 9, the pressure in the pulmonary artery was abnormally high in the resting state and increased further during exercise, while the blood flow was significantly less than 5 liters per minute per m^2 B.S. The probable causes of such pulmonary hypertension have been discussed already.

2. The final word is left to the pathologist regarding the problems of pulmonary hypertrophy in young subjects, and of the exact nature of the pathologic processes observed in the elderly subjects. The data in the children (H. W. and R. G.) who have grown to adult age with a single lung do not contradict the concept of pulmonary hypertrophy. Physiologically their lungs are perfect. Moreover, the remarkable efficiency of their lungs and that of an adult (J. Rus.) 41 years of age at the time of pneumonectomy may well be explained without recourse to this concept. The question remains unanswered as to whether the physiologic pattern presented by the two elderly subjects is related to a particular type of degenerative change occurring in the lungs of older persons after pneumonectomy, or whether they developed coincidentally a mild state of senile emphysema, as seems not improbable at their age.

3. The data presented are of more than academic interest to the thoracic surgeon. It has been shown in 2 young subjects and in one middle-aged subject that pulmonary distention following pneumonectomy does not inevitably develop in the absence of thoracoplasty. Conversely, it has been shown that thoracoplasty complicated by scoliosis may actually cause pulmonary distention. The question of optional or systematic thoracoplasty following pneumonectomy for

TABLE XVII. INFLUENCE OF THORACOPLASTY UPON DYSPNEA IN 31 CASES AFTER PNEUMONECTOMY

DIAGNOSIS	NO. OF CASES	AGE (YR.)	PNEUMONECTOMY WITHOUT THORACOPLASTY				PNEUMONECTOMY WITH THORACOPLASTY			
			NO PULMONARY DISTENTION		PULMONARY DISTENTION		NO PULMONARY DISTENTION		PULMONARY DISTENTION	
			NO. OF CASES	RESULT*	NO. OF CASES	RESULT*	NO. OF CASES	RESULT*	NO. OF CASES	RESULT*
Carcinoma of the bronchus										
Short survival (mo.)	3	39	2	–	1	–				
Long survival (yr.)	4	59			3	Good, 2 Fair, 1			1	Good, 1
Chronic pulmonary suppuration										
Children	4	12	2	Good, 2	1	Good, 1			1	Good, 1
Adults	13	39	4	Good, 4	3	Fair, 2	3	Good, 3	2	Poor, 2
Tuberculosis bronchus	7	34	1	Good, 1	3	Poor, 1 Poor, 3	1	Good, 1	2	Poor, 2
Recapitulation	31		9	Good, 7 Not estimated, 2	11	Good, 3 Fair, 3 Poor, 4 Not estimated, 1	4	Good, 4	6	Good, 2 Poor, 4

*For interpretation see text.

chronic suppuration of the lung and carcinoma of the lung has not yet been solved for lack of adequate statistics. Table XVII has been prepared in an attempt to provide such statistical data. They refer to repeated measurements of lung volume, of maximum breathing capacity, and of ventilation during exercise and recovery made in 31 patients a short time after pneumonectomy. Whenever 2 successive measurements after a six-week interval showed an increase in residual air and a reduction in maximum breathing capacity, thoracoplasty was recommended. The thoracoplasty was performed as a matter of routine in a few cases, or not performed when recommended in a few others. Estimation of the final functional result was based on the presence and the degree of shortness of breath during the recovery period of the standard exercise test.

The results may be summarized as follows:

(a) In 13 cases without thoracoplasty and pulmonary distention the final results were good in 9, fair in 1, and in 2 patients the survival period after pneumonectomy was too short to permit a proper evaluation of the result.

(b) In 11 cases without thoracoplasty but with pulmonary distention the results were good in 3, fair in 3, poor in 5. In the category of poor results are included 2 patients with tuberculosis of the remaining main bronchus.

(c) In 4 cases thoracoplasty was performed without evidence of pulmonary distention and the final results were good in all of them.

(d) Finally, in 6 cases thoracoplasty was performed to control progressive pulmonary distention, and the results were good in 2 and poor in 4. Among these 4 cases are 2 patients reported in this paper who developed scoliosis and 2 patients in whom pulmonary resection was performed for bronchial tuberculosis complicated by fibrothorax of long standing.

In conclusion it can be said that:

1. In the absence of thoracoplasty pneumonectomy is not inevitably followed by evidence of distention of the remaining lung.

2. If pneumonectomy is complicated by pulmonary distention, thoracoplasty is advisable, but the final result depends to a great extent upon the presence or absence of a pathologic process within the remaining lung.

3. Thoracoplasty may cause scoliosis and be followed by poor results due to pulmonary distention.

The observations reported in this paper concerning the dynamics of the circulation demonstrate that a state of mild pulmonary hypertension inevitably develops in the course of mild exercise, when the entire right ventricular output, circulating through a single lung, reaches an easily attainable level. In the course of strenuous activity, the blood flow in a single lung may reach very high values, which, in accordance with the general configuration of the curve relating blood flow and pressure in the pulmonary vascular bed, may result in a state of very marked pulmonary hypertension. The inference could be made from these observations that physical activity should be restricted after pneumonectomy. However, from the results of electrocardiographic studies with unipolar precordial leads[16] it seems reasonable to state that the mass of the right ventricle in the patients of this series was not increased and that therefore right ventricular hypertrophy had not developed after several years, although the subjects followed had not been restricted in their physical activity.

SUMMARY

1. The adaptation to pneumonectomy of the ventilation, the respiratory gas exchange, and the pulmonary circulation has been investigated in 16 individuals.

2. The methods of investigation used include the measurements of pulmonary blood flow and pressure, and an analysis of the alveolar ventilation-perfusion relationships, in addition to the measurements employed in previously reported studies.

3. The results are discussed in relation to age, time of study after pneumonectomy, development of pulmonary distention, and presence or absence of thoracoplasty.

4. Examination of pulmonary circulation under varying conditions of activity after pneumonectomy provides a unique opportunity to observe certain properties of the pulmonary vascular bed.

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FIBROSARCOMA OF THE BRONCHUS

Report of a Case Diagnosed by Bronchoscopy and Treated by Pneumonectomy

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PRIMARY fibrosarcoma of the lung is stated to be among the rarest of tumors.[5, 14] In earlier reports one finds the term "primary sarcoma of the lung" often without further identification as to cell type. It is apparent that the term excludes lymphosarcomas since these are primarily extrapulmonary, arising in bronchial or mediastinal lymph nodes.[7] Ball[1] in 1931 reported a fibrosarcoma primary in and replacing the left lower lobe of the lung. He reviewed the literature from 1900 to 1931 and found only thirteen well-documented cases of primary sarcoma of the lung. These included two fibrosarcomas, three spindle-cell sarcomas, six round-cell sarcomas, one "plexiform" sarcoma, and one fibrochondroadenoma with sarcomatous changes. Rosenblum and Gasul[11] in 1931 found thirteen cases of primary sarcoma of the lung reported in the pediatric literature. These included one round-cell sarcoma and one spindle-cell sarcoma; the cell type of the others was not mentioned. They added one case of their own, designated only as primary sarcoma of the lung in an infant. Of the cases collected by Rosenblum and Gasul, three had been included in the group collected by Ball.

Ellis[6] reported one case of spindle-cell sarcoma of the lung in a series of 7,272 autopsies. In the report of Massachusetts General Hospital Case 22441[14] Mallory discussed the first primary fibrosarcoma of the lung in a series of 8,000 autopsies. Three other cases have since been reported from this hospital.[15, 16, 17] Ochsner and associates,[8] in a recent report on 412 patients with primary cancer of the lung covering a period of twelve years, included two cases of fibrosarcoma in the group treated by resection; whether or not these were primary in a bronchus or diagnosed bronchoscopically was not stated in this report.

Unlike other tumors of the lung, sarcomas of any cell type have been diagnosed bronchoscopically only on rare occasions. Kahler is quoted by Pollak and associates[10] as making the earliest reference to bronchial sarcoma. In 1911 he reported a patient having a mass completely obstructing the right bronchus. A piece of the tissue coughed up was identified as myxosarcoma. Pollak and his co-workers reported a fibrosarcoma of the bronchus in a 19-year-old white man. Baum and associates[2] in 1939 reported a spindle-cell sarcoma of the bronchus in a 29-year-old white woman. In a review of the literature they were able to find only one such case previously diagnosed bronchoscopically.

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This was the case of Herrnheiser reported in 1935 (quoted by Baum[2]). Massachusetts General Hospital Case 24202[15] was a 13-year-old girl with fibrosarcoma of the bronchus diagnosed bronchoscopically. Vinson[13] has reported a lymphosarcoma of the bronchus, but this type of tumor is not included in most reviews of the subject for reasons already noted.

Ewing[7] recognized diffuse spindle-cell, small round-cell, and large round-cell sarcomas of the lung, in addition to the lymphosarcomas which form a separate group. The possibility of mistaking reparative or inflammatory tissue for round-cell or spindle-cell sarcoma was emphasized by Ewing[7] and Boyd.[5] It is thought that round-cell or anaplastic carcinoma of the bronchus was often reported as sarcoma in the earlier literature.[5, 9] Ball,[1] after excluding all cases in which the diagnosis was inadequately supported, found that primary sarcoma of the lung could be divided into two groups. The first is the diffuse or circumscribed tumor of slow progression occurring in adults and presenting, microscopically, various stages of differentiation of fibrosarcoma. The second group occurs in young individuals, is more rapidly progressive, is composed of "round" cells, and is subject to more necrosis since it is more cellular. Steward[12] has reported one case in which a mixed sarcoma occurred in the left lung of a 12-year-old girl. This tumor had some areas of spindle-cell predominance and other areas in which round cells were more numerous. No case of round-cell sarcoma diagnosed bronchoscopically has been found, probably because this tumor occurs in younger individuals and is more rapidly progressive than fibrosarcoma.

Baum and associates[2, 3] treated their patient by partial bronchoscopic removal followed by x-ray therapy. This therapy was given over a period of two years as dictated by local recurrence found bronchoscopically on two occasions. The interval between the two x-ray treatments was about twenty months. Death occurred thirty-two months after diagnosis, due to rapidly progressive extensive bilateral pulmonary tuberculosis. It was thought that the activity and caseation of the tuberculous lesions were accelerated by the heavy dosage of roentgen rays. One patient (Massachusetts General Hospital Case 24202[15]) died of massive hemorrhage from the base of the tumor during attempted pneumonectomy. The tumor caused complete obstruction of the right bronchus and was apparently detached from its base during attempt to deflate the distended, obstructed lung. Churchill, in discussing the case, pointed out the advisability of clearing the bronchus of tumor by local bronchoscopic removal preoperatively, thus making the lung more manageable at operation.

The patient reported by Pollak and associates[10] was treated by local removal of the tumor bronchoscopically, plus fulguration of its base. This sarcoma was considered on microscopic examination as "locally malignant and if properly removed should not recur." The resemblance to a sarcomatous nasal polyp was mentioned. Treatment was instituted August, 1936. The patient was well and working as a carpenter when last seen in March, 1939, having only minimal symptoms from bronchiectasis which developed distal to the tumor.

CASE REPORT

Illness at Time of Admission.—A 29-year-old college student was admitted to this hospital Dec. 25, 1947, because of severe pain in the left side of the chest, dyspnea, cough, and wheezing. He had lost 23 pounds in the past five months. Symptoms began in July, 1946, with mild dyspnea on exertion, becoming progressively worse until September, when wheezing and occasional small hemoptyses were noted. Cough was mild and not productive except when hemoptysis occurred. Bronchoscopy at this time was reported as negative. Ten days prior to admission the patient developed chills and fever, with severe pain in the left side of the chest. Bronchoscopy was repeated but nothing was found, and he was transferred to this hospital.

Physical Examination.—Physical examination revealed a well-developed, undernourished white man, not acutely ill. He was slightly dyspneic. Skin was pale and showed some evidence of recent weight loss.

Examination of the chest revealed significant flattening of the lower half of the chest on the left, with a marked lag on deep inspiration. Tactile fremitus was diminished in the upper half and absent in the lower half of the left side of the chest. There was dullness to percussion over the lower half on the left, with diminished to absent breath sounds over the entire left side. A definite wheeze was heard over the left lower lung field on deep inspiration. There was a shift to the left of the lower mediastinum. There were no abnormal findings over the right side of the chest. The heart was normal. The remainder of the physical examination was essentially negative.

Roentgenogram of the chest revealed pleural thickening with subpleural fibrosis over the right apex, and atelectasis of the left lower lobe.

Serum examinations for syphilis were negative. Blood and urine analyses revealed no abnormalities. Sputum examinations were repeatedly negative for acid-fast bacilli. Blood chemistry was normal.

Bronchoscopy done Dec. 29, 1947, showed the left main stem bronchus almost completely occluded by a round, smooth, shining, nonulcerated, dark red, fairly firm tumor, attached to the medial wall of the bronchus about ½ cm. distal to the presenting edge of the carina. A portion of the tumor, sufficiently large to establish a free airway, was removed for biopsy without excessive bleeding. The trachea and right bronchial tree were normal.

Pathologic Report.—The pathologist* gave the following report on the bronchial biopsy. Microscopic examination of tissue obtained by bronchial biopsy revealed a small portion of the specimen to be covered by normal-appearing bronchial mucosa, while in another area the mucosa had undergone a pronounced squamous-cell metaplasia. Immediately beneath, but not involving the mucosa, was a pleomorphic cellular neoplasm composed of loosely arranged, spindle-shaped fibroblasts. The fibroblasts possessed delicate cytoplasmic processes and, with phosphotungstic acid hematoxylin stain, demonstrable fibroglia fibrils. The cells were separated by delicate strands of collagen. These cells in occasional areas were arranged in loose nests, vaguely suggestive of whorls, while in most areas the cells remained more discrete with no indication of pattern arrangement. While the cells possessed large hyperchromatic nuclei with a reticular meshwork of nuclear chromatin, there was no indication of mitotic activity. The neoplasm had a rich vascular supply, but in no area could invasion of vessels be demonstrated. Diagnosis was fibrosarcoma of bronchus.

Following bronchoscopic removal of a portion of the tumor for biopsy, the lower lobe atelectasis cleared almost entirely and the mediastinal silhouette returned to normal position.

On Jan. 14, 1948, a left pneumonectomy was done, with division of the main bronchus at the level of the carina. The individual ligation technique was used. Except for a small, firm, discrete subpleural nodule in the mid-portion of the lateral aspect of the upper lobe, the lung presented no gross abnormality. There were no pleural adhesions. There were no grossly enlarged or abnormal hilar nodes encountered. One slightly enlarged node was found in the angle at the bifurcation of the trachea.

*Dr. O. J. Wallenman, Jr.

Gross Findings.—The gross specimen consisted of a collapsed left lung weighing 250 grams and all of the left main bronchus. At a point 5 mm. from the carina the essential findings were small, granular, hemorrhagic lesions of the bronchial mucosa. The mucosa proximal to and distal to the tumor, as well as throughout the entire bronchial tree, was intact and glistening gray. No peribronchial masses were present. The lung parenchyma was not remarkable except for a solitary, subpleural 2 mm. nodule situated in the lateral aspect of the mid-portion of the upper lobe. The hilar lymph nodes were not enlarged and on section did not appear remarkable. A separate node removed from the bifurcation of the trachea measured approximately 7 by 4 by 4 mm. and on section had a minute, central, caseous area surrounded by normal-appearing lymph node.

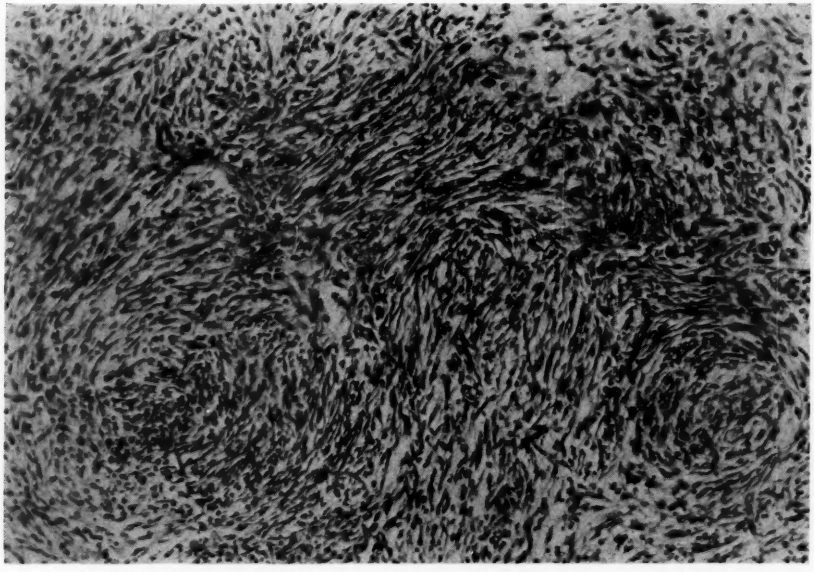

Fig. 1.—Bronchial biopsy showing whorling and interlacing arrangement of fibroblasts. (Hematoxylin and eosin stain, magnification ×180.)

Microscopic Findings.—Microscopic examination of sections removed from the granular portion of the left main bronchus described in the gross findings revealed a polypoid mass covered with metaplastic bronchial mucosa projecting into the lumen of the bronchus. Immediately beneath the mucosa were loosely arranged spindle cells separated by strands of collagen and what appeared to be edema fluid. The spindle cells became more numerous and compact at the base of the polyp, and in this area and deeper in the submucosa and muscularis of the bronchus, the cells tended to lose their spindle shape characteristic; the nuclei were much larger, more hyperchromatic, and in some areas the cells appeared oval to round with the nucleus occupying three-fourths of the cell structure. This more anaplastic appearance was a definite gradient from the more mature fibroblasts comprising the polyp. Although the cells appeared anaplastic and less differentiated than seen in the biopsy specimen, mitotic activity was found with extreme difficulty. In no area was there attempted differentiation into the glandular structures, sheets of cells, or strands reminiscent of bronchial mucosa origin. The tumor was richly vascularized, and in a few areas chronic inflammatory cells were seen, as well as an occasional focus of lipoid laden macrophages (Fig. 1). Microscopic examination of the nodule described in the gross findings as situated

beneath the pleura revealed this to be an encapsulated benign chondroma situated adjacent to a small bronchiole in the lung parenchyma. This chondroma was surrounded by a moderately dense fibrous tissue capsule and was composed of mature hyaline cartilage. The adjacent lung parenchyma, as well as multiple sections from various portions of both lobes, showed partial atelectasis without inflammatory reaction. There was no evidence of neoplastic tissue in the lung parenchyma. Microscopic examination of the accompanying lymph node described in the gross findings revealed an encapsulated eosinophilic amorphous material occupying the central portion of the node. The capsule was composed of dense, fibrocollagenous tissue without evidence of cellular inflammatory reaction. Microscopic examination of other lymph nodes removed from the hilus revealed heavy carbon pigmentation, but otherwise were not significantly altered. Diagnoses: (1) Fibrosarcoma, left main bronchus; (2) chondroma, benign; (3) tuberculous lymphadenitis, encapsulated.

The patient had an uneventful postoperative course, and immediately prior to discharge from the hospital on Feb. 3, 1948, bronchoscopy revealed a well-healed suture line on a plane with the carina and the left wall of the trachea. The mucosa appeared normal. Follow-up examination on April 5, 1948, and again on Sept. 1, 1948, seven and one-half months after resection, showed a normal bronchial mucosa. The patient had no complaints, was felling well and attending school.

COMMENTS

It is apparent, in the light of the infrequency with which primary sarcoma of the bronchus is encountered, that no single plan of treatment can be formulated on the basis of experience. The spindle-cell sarcoma reported by Baum and associates was treated by partial bronchoscopic removal followed by x-ray therapy. Death occurred thirty-two months later from extensive bilateral pulmonary tuberculosis. Local recurrence was observed on two occasions prior to death. This case would suggest that x-ray therapy could present an unwarranted risk in any patient in whom treatment by resection is not contraindicated. The patient with fibrosarcoma of the bronchus discussed by Mallory died of hemorrhage from the base of the tumor during attempt at pneumonectomy. The fibrosarcoma reported by Pollak and associates was treated by local removal and fulguration of the base. They reported that the patient was well three years later.

Our decision to elect pneumonectomy as the treatment of choice in the case reported here was based upon uncertainty as to the depth of invasion of the bronchial wall, although no extrabronchial extension could be demonstrated roentgenologically. A free airway was established at the time of partial bronchoscopic removal and persisted throughout the resection. Subsequent microscopic examination of the base of the tumor showed extension of the neoplasm between the cartilaginous rings to involve the entire thickness of the bronchial wall. Local removal and destruction by fulguration of anything less than the full thickness of the bronchial wall in this case would have failed to eradicate the tumor. Since it is conceivable that fibrosarcoma may simulate bronchial adenoma in its manner of growth, that is, by assuming a "dumbbell" shape, we feel that pulmonary resection should be carried out proximal to the site of the tumor. The amount of pulmonary tissue to be sacrificed would then depend upon the location of the neoplasm.

SUMMARY

1. Primary sarcoma of the lung is in itself a rare disease, and primary involvement of a bronchus is exceptionally so.

2. A brief review of the American literature indicates that a total of thirty-one cases of primary sarcoma of the lung have been reported. We are able to find only six reported cases of sarcoma primary in the bronchus. The treatment of these has not been uniform.

3. The treatment of primary sarcoma of the bronchus is discussed.

4. A case of primary fibrosarcoma of the bronchus, diagnosed bronchoscopically and treated by pneumonectomy is presented in detail.

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FIBROSARCOMA OF THE BRONCHUS

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DESPITE the extensive experience with pulmonary neoplasms in the past fifteen years and despite the large series of cases that have been reported from various clinics, primary sarcoma of the lung in general and primary intrabronchial fibrosarcoma in particular must still be regarded as lesions of considerable rarity. At the turn of the century Seydel[30] reviewed a large number of cases reported up to that time. Among these were many "round-cell sarcomas" (probably mostly undifferentiated bronchial carcinomas or lymphosarcomas of the mediastinum with extension to the lung). There were also several "spindle-cell sarcomas" mentioned, but we have been unable to verify any of them as primary fibrosarcomas of the bronchus from the data available in the reports. In this connection it is well to recall Stout's[33] statement that "it is an utter waste of paper to report a tumor by this title [spindle cell sarcoma] unless the description and illustrations are so good that an expert oncologist, aided by the clinical history, can recognize the true nature of the growth from them."

A similar lack of adequate description makes it impossible to confirm as primary bronchial fibrosarcoma a single one of the cases of sarcoma of the lung which Adler[1] listed in his book published in 1912. Moreover, Adler stated that he had never seen a primary sarcoma of the lung in his personal experience and called attention to the difficulty often encountered in distinguishing very undifferentiated carcinomas of the lung (including the so-called "oat-cell" tumor) from sarcomas. Because of the failure of many authors to make this important differentiation, their reported cases have had to be discarded as unsubstantiated.

Edwards[8] noted that in the late 1920's there was a rapid disappearance from the literature of reports of large numbers of cases of primary sarcoma of the lung because of Bernard's reiteration that a more careful study would separate the very undifferentiated epithelial tumors from the sarcomas. Many reports are still encountered, however, in which the criteria for establishing the diagnosis of sarcoma are incompletely described.

Stout[33] has done much to clarify the confused subject of fibrosarcoma, and it would be well to set down his criteria for this diagnosis before evaluating the individual case reports. All tumors except those composed of fibroblasts which produce collagen and reticulin fibers (the latter being wrapped around the individual tumor cells in a characteristic manner) have been excluded in this report. The variation in degree of production of these fibers and the lack of collagen in the more undifferentiated fibrosarcomas are pointed out. The parent cells are almost always fusiform when cut along the long axis and are dis-

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tributed in bundles or cords which interlace in gentle curves. Occasionally areas are found in which the bundles abruptly change direction giving the appearance of whorls. Stout thus includes under the heading of fibrosarcoma those tumors which others have termed "neurofibrosarcoma," and to this classification we emphatically adhere.

In the true fibrosarcoma mitoses are rare, for most of these tumors are well differentiated and slowly growing. The finding of giant cells in a true fibrosarcoma is rare and if any significant number of them are seen, a careful study generally identifies the tumor as some other form of sarcoma (liposarcoma, rhabdomyosarcoma, or leiomyosarcoma). Stout recognizes only two forms: the well-differentiated fibrosarcoma with well-developed collagen and reticulin fibers, little pleomorphism or hyperchromatism, and rare mitotic figures; and the undifferentiated fibrosarcoma which has closely packed cells with hyperchromatism, pleomorphism, many mitotic figures, few collagen fibers, and only delicate reticulin fibers.

Recently, several papers describing large series of pulmonary neoplasms have appeared in which passing mention is made of sarcoma. Thornton, Adams, and Bloch[34] spoke of one patient with "sarcoma," otherwise unclassified, which was found inoperable at exploration, and was given x-ray therapy but later died. These same authors[5] subsequently listed 5 unspecified sarcomas discovered among 91 intrathoracic tumors in routine chest fluoroscopy of 15,000 patients in the outpatient department of the University of Chicago Clinics. O'Brien, Tuttle, and Ferkaney,[23] in a report of solitary shadows in the lung, mentioned one patient with "sarcoma" who has since died; no further details are given. Edwards[8] reported three cases of "sarcoma, all ossifying" in his series of intrathoracic neoplasms, but we can only speculate as to the exact nature of these tumors. The follow-up on these patients revealed that two were operated upon with one postoperative death and one survival for two and one-half years at the time of the report; the third was inoperable but was alive without evidence of disease two and one-half years after a course of x-ray threapy. Harrington[10] mentioned six cases of sarcoma of the lung in which the patients were treated by pneumonectomy, one of whom had survived five years without evidence of recurrence at the time of his report in 1931. The other patients were all dead within two and one-half years of operation.

In their most recent report of patients with pulmonary neoplasms submitted to operation, Oehsner, DeBakey, and associates,[24] have had all their microscopic sections reviewed by Dunlap. They had previously reported two cases of fibrosarcoma, but the more recent appraisal placed these two tumors in the class of undifferentiated carcinomas. One tumor, however, still considered a "neurofibrosarcoma," was removed by pneumonectomy with a survival of twelve years. Stout would probably classify this as a fibrosarcoma, but unfortunately for our present purpose the exact site of origin of this tumor is not given. It is the only case in the literature with apparent cure following pneumonectomy, although Neuhof and Aufses[22] cited an eleven-year survival

after pneumonectomy for a neoplasm that is not described except by the general term sarcoma. In another larger series of cases Jackson[11] mentioned six sarcomas which were all seen as endobronchial growths and diagnosed by bronchoscopic biopsy. Only one of these was a "spindle-cell sarcoma," and there was no further information as to treatment, follow-up, or postmortem. As no photomicrographs or histologic description were available this case has also been excluded.

In recent years the most comprehensive paper on the subject of primary pulmonary sarcoma is that of Ball.[2] In his review of the literature he found fourteen cases which he considered verifiable in addition to his own. Among these were six cases diagnosed as "round-cell sarcoma," a term which probably implies that they were lymphosarcomas. Since this neoplasm is not being considered in this report, and since they cannot be classified more accurately from the published data, they have been eliminated. Five others, including those of Edwards,[7] Stevens,[31] and Pritchard[27] were found to have inadequate histologic study and description. Another was termed a "fibrochondroadenoma with osteoid tissue." This leaves only the cases of Boschowsky[6] and Ball,[2] both of which have adequate histologic description to substantiate the diagnosis of fibrosarcoma. These tumors, however, occupied almost the entire lung and their site of origin, whether from the pleura or pulmonary parenchyma, is not clear. From the descriptions it is impossible to include them with polypoid fibrosarcomas of the bronchus. Other cases which were discarded for the same reasons are those of Ellis,[9] Mallory,[18, 21] Lyssunkin,[16, 17] Scheidegger,[29] Stohr and Sachs,[32] and Klemperer and Rabin[13] although they are well-documented fibrosarcomas of the lung or pleura.

Other reports of tumors which were diagnosed as fibrosarcoma primary in the lung have been reviewed but have been found deficient in one or more respects for inclusion with verified cases. Thus, the reports of Rolleston and Trevor[28] and Lange[14] must be discarded because of inadequate histologic description and that of Mallory[20] because the pulmonary tumor was not definitely proved as primary, although the histologic description appears to be adequate.

This leaves only five cases from the entire medical literature (see Table I) which can be considered primary fibrosarcomas of the bronchus. All are polypoid bronchial tumors with varying extension into the lung parenchyma and have either good histologic descriptions or photomicrographs from which it is possible to verify the diagnosis.

CASE 1 (Baum[3, 4]).—The tumor was removed through the bronchoscope followed by x-ray therapy. The author stated that there was no evidence of persistent tumor at the autopsy of this patient who died of tuberculosis two years and nine months after the onset of illness, but one wonders whether the "bundles of apparently fibrous tissue running in various directions and abutting against necrotic tuberculous tissue" found at the site of the original tumor do not represent persistence. It would be unusual indeed in view of Stout's experience[33] to find sterilization of a fibrosarcoma by x-ray therapy.

CASE 2 (Johns and Sharpe[12]).—No treatment was given, and the patient died of respiratory complications fifteen months after the onset of symptoms.

TABLE I. VERIFIED CASES OF FIBROSARCOMA OF THE BRONCHUS

AUTHOR	AGE, RACE, SEX	DURATION OF SYMPTOMS	ANATOMIC FINDINGS AND TREATMENT	MICROSCOPIC FINDINGS	RESULTS
Baum et al[3, 4]	29, W, F	1½ mo. cough, pain in chest, weight loss	Bronchoscopy: Just below carina in right main stem bronchus a soft, polypoid mass was found and removed by suction. Further bronschoscopic removals and total of 18,630 r x-ray therapy over a period of 2½ yr.	Ciliated bronchial epithelium with underlying fibrosarcoma. Photomicrographs substantiate this. No silver stain	Death from tuberculosis 2 yr. and 9 mo. after onset of illness
			Postmortem: At site of former tumor in right main stem bronchus a minute firm nodule was found. There was widespread chronic tuberculosis with cavitation. No evidence of metastases elsewhere	Nodule was made up of bundles of apparently fibrous tissue running in various directions abutting against necrotic tuberculous tissue	
Johns and Sharpe[12]	18, W, M	2 mo. cough, hemoptysis, weight loss	No treatment given. Postmortem: Right lung almost entirely replaced by a friable tumor with a thin rim of atelectatic lung tissue around it. Tumor extended into and along right main stem bronchus to 1.5 cm. above carina. It also grew in lumen of right pulmonary vein into auricle. No metastases elsewhere	Fibrosarcoma with numerous mitotic figures. Silver stain reveals fine reticulin fibers around individual cells	Death from pulmonary disease 15 mo. after onset of symptoms
Lewis[15]	14, W, M	1 mo. dyspnea, cyanosis, pain, cough	Bronchoscopy: Orifice of right main stem bronchus was filled with a soft growth attached up to carina. Bronchoscopic removal and x-ray therapy amounting to 6,353 r	Fibrosarcoma with whorl arrangement and considerable pleomorphism. No silver stain	Tumor was persisting 4 mo. later but well with negative x-ray 2½ yr. after onset

Mallory[19]	13, W, F	2 mo. cough, pleuritic pain, weight loss	Bronchoscopy: Within right main stem bronchus a 1 by 1.5 cm. mass. Postmortem: Major portion of tumor found lying free in bronchus with evidence of tumor remaining in bronchial wall	Fibrosarcoma growing at moderate rate and invading bronchial wall. No statement about invasion of parenchyma. No silver stain	Died of intrapulmonary hemorrhage during exploratory operation
Pollack et al[26]	19, W, M	7 mo. cough, pain, fever, wheezing, weight loss	Bronchoscopy: Left main stem bronchus obstructed 1 in. below carina by soft mass 2 to 3 cm. in diameter. Another similar mass opposite it on bronchial wall. Bronchoscopic removal and fulguration on 5 occasions	Fibrosarcoma of bronchus confirmed by Dr. F. W. Stewart of Memorial Hospital N. Y. No silver stain	Well without bronchoscopic, bronchographic, or x-ray evidence of recurrence 31 mo. later. Well at the end of 6 yr.
Black	46, W, F	9 mo. cough, fever, weight loss, hemoptysis	Operation: Left pneumonectomy. Polypoid 1.5 cm. tumor arising in basal divisions of lower lobe bronchus. Tumor extends through bronchial wall and within 2 mm. of mediastinal pleura; 12 lymph nodes negative. Large abscess in lateral portion of lower lobe with tumor in wall. Postmortem: Persistent tumor in mediastinal glands, bronchial stump and pericardium	Fibrosarcoma, moderately undifferentiated with pleomorphism and mitotic figures. Wilder stain shows fine reticulin fibers around individual cells	Died of recurrent tumor 6 yr. and 5 mo. after operation

CASE 3 (Lewis[15]).—The tumor was removed through the bronchoscope with subsequent radiotherapy. There was persistent tumor four months after treatment, but a recent letter from the author stated that the patient was well with a negative roentgenogram two and one-half years after the institution of treatment.

CASE 4 (Mallory[19]).—In only this one case was an attempt at pulmonary resection made, but the patient died of intrabronchial hemorrhage on the operating table.

CASE 5 (Pollack, Cohen, and associates[26]).—The tumor was removed through the bronchoscope. Thirty-one months after removal and fulguration, which had been performed in 1936, there was no evidence of persistent disease by roentgenogram, bronchogram, or bronchoscopy. A recent personal communication from one of the authors (Cohen) stated that the patient was lost to follow-up study in 1942, at which time he was entirely well. This survival of more than six years is surprising, but owing to the known slow evolution of some fibrosarcomas, even this length of observation may not be adequate to determine the ultimate outcome.

Despite the apparent success of endobronchial forms of treatment in the three cases mentioned, it is not a form of therapy to which we subscribe even though the fibrosarcoma may be a slowly growing tumor. In order to remove all of the neoplasm we feel that the treatment must be by pulmonary resection as in all pulmonary neoplasms. The case reported here illustrates the advantage of pneumonectomy, since the patient had palliation for over six years. In spite of the unfavorable final outcome, it seems justifiable to believe that a cure by radical surgery may be expected in this type of tumor provided it is seen in the early stages of development.

CASE REPORT

M. A. McC. (History No. 93545), a 46-year-old white woman, entered Barnes Hospital on Nov. 12, 1941.* She had a history of several attacks of "flu" nine months previously, characterized by coryza, cough, general malaise, and a low-grade fever. Four months before admission she had another respiratory infection with cough, fever, and small hemoptyses. Treatment with sulfonamides resulted in rapid clearing of the symptoms, but one month later the roentgenograms showed no change in the shadow in the left lower lobe which had been noted previously. Bronchoscopic biopsy was performed, and the husband was informed that the patient had a malignant growth. Repeated sputum examinations and guinea pig inoculations were negative for acid-fast bacilli. Two thoracenteses failed to demonstrate pleural fluid. There was a loss of weight of 10 pounds in four months, but no chest pain at any time.

Past History.—Noncontributory.

Family History.—A maternal aunt died of carcinoma of the breast, and a maternal uncle had carcinoma of the prostate.

Physical Examination.—The patient was a thin, fairly well-developed woman appearing chronically ill but in no acute distress. Vital signs were within normal limits except for pulse of 120. The trachea was in the midline, but the chest seemed to have increased fullness in the left upper region anteriorly with diminution of expansion at the base. There was decreased fremitus and flatness to percussion with absent breath sounds over the entire surface projection of the left lower lobe. No râles were heard, and the right lung field was clear. The remainder of the examination was within normal limits.

Roentgenogram.—The mediastinal structures were in the midline and complete opacity of the lower half of the left lung field as high as the anterior end of the fourth rib was seen. The right lung was clear.

Bronchograms.—Left main stem and left upper lobe bronchi were well filled, but only the apical division of the lower lobe bronchus contained any opaque substance.

*Referred by Dr. John F. Dicks of New Orleans, La.

Fluoroscopy.—There was normal motion of both leaves of the diaphragm.

Laboratory Examination.—Laboratory examination was noncontributory.

Bronchoscopy.—In the left main stem bronchus approximately 1 cm. distal to the upper lobe orifice a polypoid tumor was found completely blocking the lower lobe bronchus. A biopsy showed the obstruction to be due to a very cellular neoplasm.

Operation.—Nov. 17, 1941, under cyclopropane anesthesia, the left sixth rib was resected.* The tumor was located in the lower lobe together with a thick-walled abscess in the lateral peripheral portion. The adhesions between the lower lobe and chest wall were divided without entering the abscess, and the lung was removed, employing the individual ligation technique.

Gross Pathology (Surgical Pathology No. 39049) (Fig. 1).—The surfaces and parenchyma of the left upper lobe were normal. The lingula and lower lobe presented thickened pleura with fibrous adhesions and consolidation. On opening the bronchus a polypoid tumor measuring approximately 1.5 cm. in diameter was found arising from the wall of the lower lobe bronchus occluding it completely. It extended into the subdivisions of the lower lobe bronchus and through the bronchial wall into the surrounding parenchyma. At the inferior portion of the hilum the tumor was growing within 2 mm. of the pleura but had not reached it in any area. The free part of the intrabronchial portion of the tumor reached to within 2.5 cm. of the line of resection.

Distal to the tumor the lower lobe was completely consolidated with many areas having the mottled yellow appearance suggestive of lipoid deposition. At the basal peripheral portion of the lobe there was a ragged abscess cavity measuring 9.0 cm. in diameter and containing necrotic material. The upper lobe was entirely normal. Lymph nodes did not appear to be invaded grossly by the tumor.

Microscopic Pathology.—The predominantly intraluminal character of the tumor and its extension through the bronchial wall toward the pleural surface is illustrated in Fig. 2.† Sections from the wall of the abscess cavity also showed tumor. Fourteen lymph nodes taken from the region of the upper and lower lobe bronchi and two from medial to the main stem bronchus were negative.

The tumor was composed of spindle-shaped cells (Fig. 3) arranged in whorls in some areas. There was moderate variation in the size of the nuclei, some being more rounded than others, and a moderate number of mitotic figures were seen (Fig. 4). Connective tissue stain revealed very little intercellular stroma, and the Wilder stain demonstrated a fine reticulin network wrapped around the individual cells (Fig. 5). The impression was that of a moderately undifferentiated fibrosarcoma arising as a polypoid tumor in the bronchus without demonstrable metastasis or extension beyond the lung, although it had broken through the bronchial wall and invaded the lung parenchyma.

Follow-up.—The postoperative course was marked by a temperature elevation which persisted in the neighborhood of 38° C. for five weeks with occasional spikes to 39.5° and 40° C. Accompanying this there was leucopenia of about 6,000 with a relative lymphocytosis (35 to 50 per cent). Repeated search for malarial parasites because of the fever and enlarged spleen were negative. Pleural fluid cultures were likewise negative, and the temperature elevation was never satisfactorily explained.

After return to her home the patient made a complete recovery except for two brief unexplained febrile episodes occurring two and four years after operation. A letter from her in July, 1947, stated that she was doing housework and feeling well. She spoke of some cough "due partly to allergic irritation of nose and throat" but there was no pain or dyspnea at that time. X-ray examinations of the chest in March and April, 1947, at the Touro Infirmary in New Orleans‡ because of returning chest complaints revealed a patchy pneumonic process in the right lung field. However, follow-up films in September, 1947, showed complete clearing of this infiltrate and no other departures from the normal.

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*By Dr. Evarts A. Graham.

†These slides, as well as those submitted from the autopsy material, have been reviewed by Dr. Lauren V. Ackerman, Associate Professor of Surgical Pathology, Washington University School of Medicine.

‡Courtesy of Dr. W. R. Arrowsmith, Ochsner Clinic, New Orleans, La.

She remained well until Christmas, 1947, at which time she had an illness diagnosed as "influenza" with afternoon fever as high as 102° F. In March she was hospitalized at the Touro Infirmary at which time the liver was found to be enlarged with a 48 per cent bromsulfalein retention. A needle biopsy of the liver was reported as essentially normal.

Her course was rapidly downhill, and she died April 22, 1948, in the Ochsner Medical Foundation Hospital in New Orleans. Terminally there was paroxysmal auricular tachycardia with a rate of 140-150, and respiratory distress which responded to digitalis, quinidine,

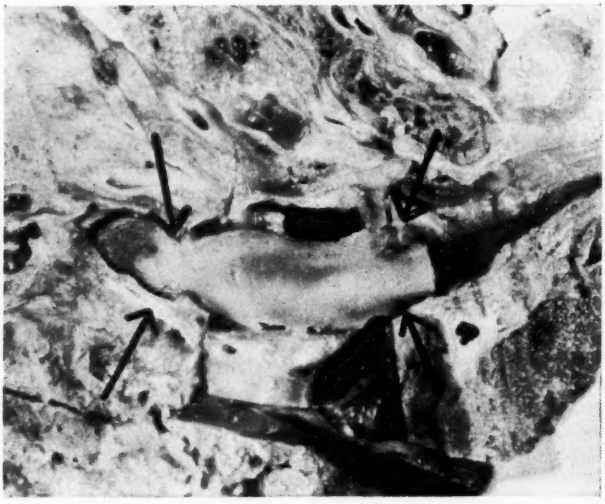

Fig. 1.—Photograph of gross specimen showing polypoid tumor in lower lobe bronchus. Hilus is to the right.

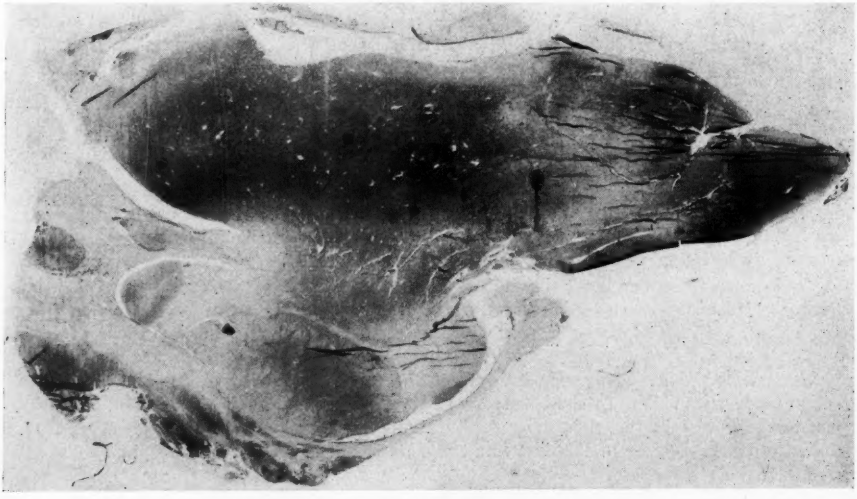

Fig. 2.—Low-power photomicrograph showing origin of tumor from the bronchus in the lower half of the picture (×6).

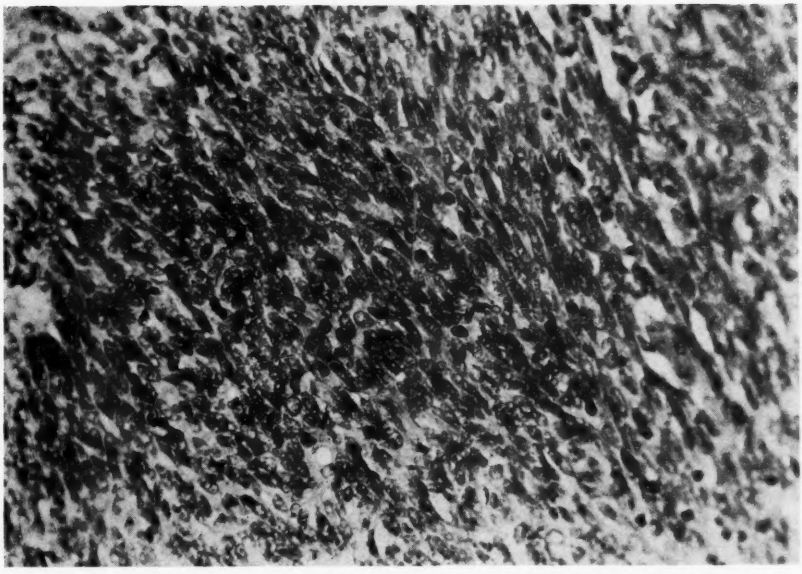

Fig. 3.—High-power photomicrograph of original tumor showing closely packed fusiform cells with moderate pleomorphism, mitotic figures, and very little intercellular material (×440).

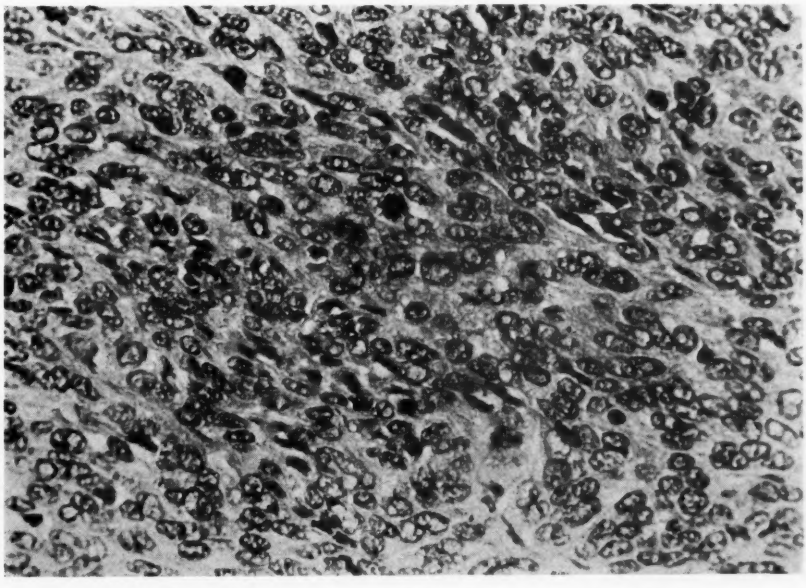

Fig. 4.—Photomicrograph from another area of origional tumor which demonstrates mitotic figures and rounded nuclei (×660).

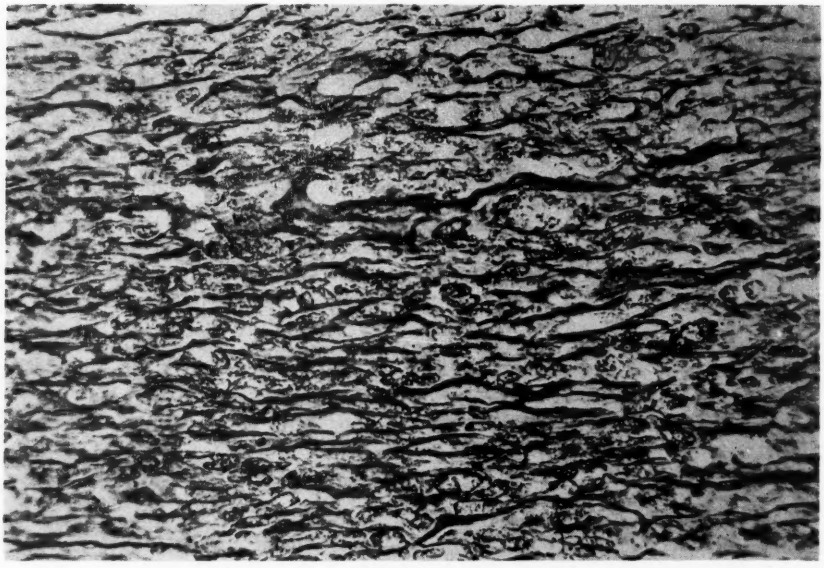

Fig. 5.—Wilder stain reveals fine network of reticulin fibers wrapped around the individual tumor cells (×600).

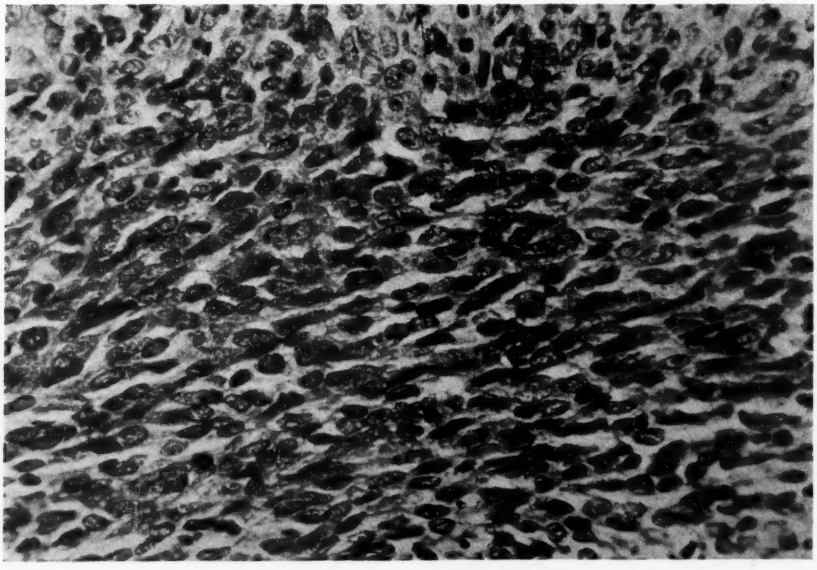

Fig. 6.—Photomicrograph of recurrent tumor at higher power reveals it to be identical with original (×660).

aminophylline, blood, and oxygen. The electrocardiogram revealed definite evidence of myocardial disease. The liver was enlarged 4 cm. below the costal margin, and there was 2 plus edema of the extremities. Just prior to death there was atelectasis of the right lower lobe, and bronchoscopy revealed external compression of the right main stem bronchus.

She had survived six years and five months after pneumonectomy and seven years and two months after the onset of symptoms, most of this time in good health.

*Post-mortem.**—The mediastinum was shifted markedly to the left and the right pleural cavity contained 1,500 c.c. of serosanguineous fluid. The left pleural cavity was completely obliterated by dense fibrous adhesions. Posterior to the carina there was a large irregular mass which was identified as degenerating tumor in lymph nodes and which extended around the left bronchial stump. It also invaded the hilar area of the right lung, compressing the right main stem bronchus. The tumor mass measured 10 by 8 by 6 cm. and invaded the posterior wall of the left atrium as far as the endocardium, as well as the wall of the esophagus. There was marked distention of the pericardial sac with 750 c.c. of bloody fluid.

Microscopic examination revealed that the tumor was identical with that removed at operation. A representative section is seen in Fig. 6. There were no metastases in the liver, adrenals, pancreas, or elsewhere outside the thorax.

DISCUSSION

That this neoplasm is a rarity in the literature must be obvious from the small number of cases that have been found, but it is equally apparent that this tumor has behaved in a manner similar to fibrosarcomas elsewhere, growing slowly, spreading only by local invasion, and not producing distant metastases. Womack and Graham[35] have long held the view that many bronchial and pulmonary tumors arise from the aberrant development of embryologic lung buds and that the resultant neoplasms can therefore consist of derivatives of either entodermal or mesodermal elements in the bronchi or a combination of these. The so-called bronchial adenoma can thus be considered an epithelial variant and the chondroma a mesodermal expression. The neoplasm that is the subject of the present report is believed, from a study of many sections including those from the postmortem, to be a tumor derived from mesodermal tissue only and to be a classical fibrosarcoma. As such it is consistent with this theory of origin of some of the primary bronchial neoplasms, and illustrates a tumor of moderate malignant potentialities.

SUMMARY AND CONCLUSIONS

1. A case of primary fibrosarcoma of the bronchus treated by pneumonectomy is reported. Death occurred from persistent tumor in the thorax six years and five months later.

2. Review of the literature has revealed only five verifiable cases of a similiar nature. Although three of these had apparent cure following bronchoscopic removal of the tumors, in one case there was question of persistence at autopsy and in the other two, owing to the known slow evolution of the tumor, the two and one-half and six year follow-up periods, respectively, may not be adequate to determine the ultimate outcome.

3. It is believed that pulmonary resection is the only rational treatment of these neoplasms.

*Description of post-mortem examination and microscopic slides, courtesy of Dr. J. C. Henthorne of the Ochsner Medical Foundation, New Orleans, La.

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EXPECTORATION OF A FIBROSARCOMA

Patient Well Four Years Later

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IN RECENT years considerable attention has been given to microscopic examination of expectorated material with a consequent advance in the study of intrapulmonary cancer. In 1945 Samper* reported the case of a patient who coughed up tissue which proved to be a grade 3 squamous-cell epithelioma. Bronchoscopic and lipiodol studies failed to reveal the source of the tumor but four years later, after pneumonectomy, the origin of the cancer was found in the left main bronchus.

The following case is reported because it is unusual and re-emphasizes the importance of microscopic examination of coughed up material.

C. M., a white female, aged 13 years, was referred to the Massachusetts Memorial Hospitals in April, 1944. Except for a mild attack of rheumatic fever she had enjoyed good health until about six weeks before admission to the hospital. At this time she noted a gradual onset of cough associated with intermittent wheezing and productive of slight amounts of yellowish sputum. Three weeks later she experienced a fairly severe and steady nonpleuritic pain in the left side of the chest, close to the sternum. One week before admission, shortly after a bout of strenuous exercise, she coughed up a lump of tissue "about the size of an almond" and then approximately one cupful of bright red blood. Following this episode cough and wheezing disappeared. The tissue was submitted to the Leary laboratory by her family physician and the following was reported: The specimen consisted of a gray-red mass, measuring 1.5 by 1 cm., showing an external smooth gray surface and no demonstrable stalk or base. On section the tissue was uniformly gray-red and resembled fish flesh. Microscopic diagnosis was fibrosarcoma. The patient was then referred to the hospital seven days after the episode of expectoration and was completely asymptomatic.

Physical examination revealed a well-developed and well-nourished young white girl in no apparent distress. Nasopharyngoscopy results were negative. The trachea was in the midline and there were no cervical or axillary nodes. The lung fields were clear and resonant and the remainder of the examination was likewise not remarkable.

Laboratory work showed repeated urinalyses negative. On examination of the blood the level of hemoglobin was 15 Gm. per 100 c.c., leucocytes numbered 9,750 per cubic millimeter, and the differential white cell count was normal. Stools tested gave negative results with gum guaiac. Fluoroscopic examination of the chest showed normal respiratory movement of both diaphragms. X-ray films of the chest taken in inspiration and expiration were also within normal limits. Roentgenograms of skull and sinuses were negative. The hospital course was afebrile and asymptomatic. Bronchoscopic examination was twice performed† and revealed a normal carina with a heaping up of tissue just inside the left main stem bronchus on the mesial wall. Only a small biopsy was possible because of the location of the lesion and examination of this tissue revealed granulating fibromuscular tissue.

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*Samper, R.: Expectoration of Carcinomatous Tissue Without Localizing Signs in Four Subsequent Years, Pneumonectomy: Report of a Case, Proc. Staff Meet., Mayo Clin. 20: 341, 1945.

†By Dr. John Strieder.

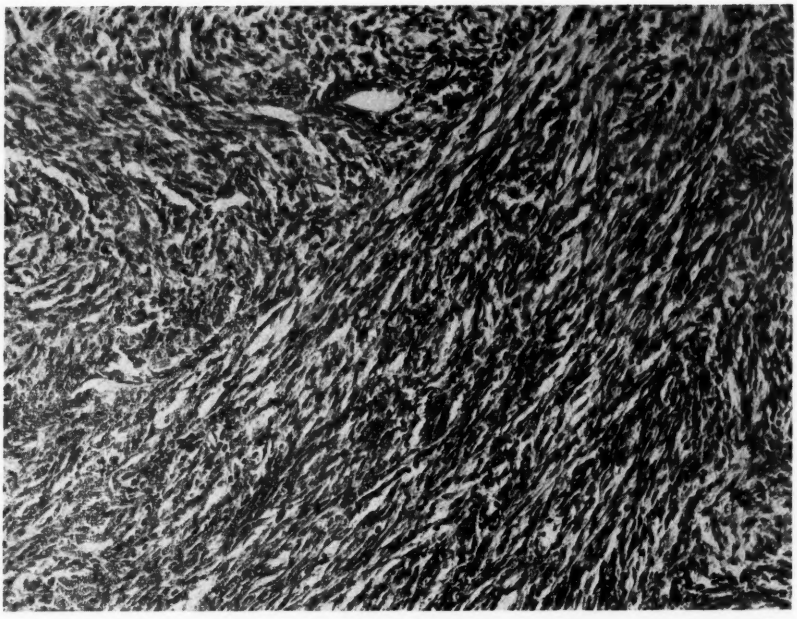

Fig. 1.—Low-power view showing whorled appearance with typical fusiform cells. A tumor giant cell is noted in the center of the field. (Hematoxylin and eosin, ×200.)

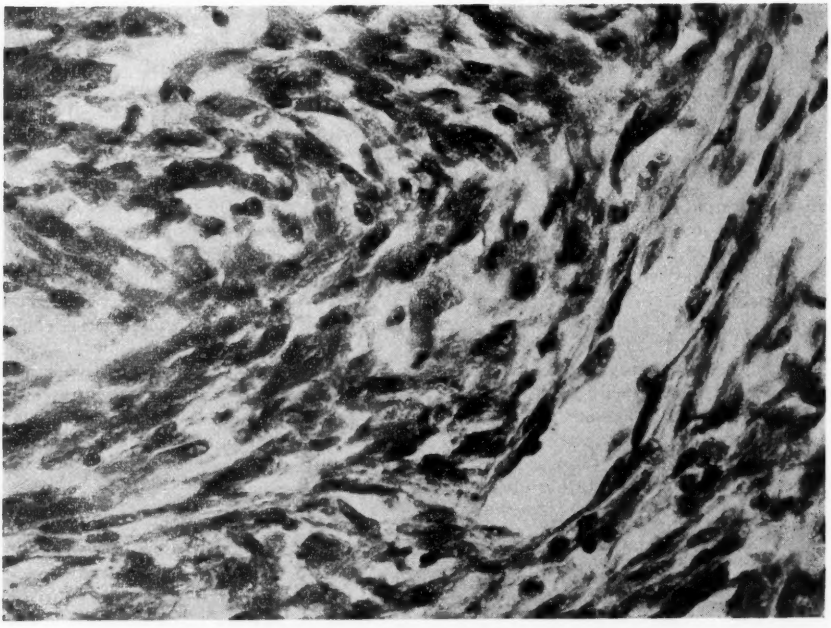

Fig. 2.—Higher magnification displaying two mitoses. The cells are fusiform with variability in nuclear size and staining, and possess a finely granular cytoplasm. A capillary courses through the section. (Hematoxylin and eosin, ×800.)

A review of the original section from the tumor mass showed that it was roughly 2 cm. in diameter and composed of dense interlacing strands of moderately anaplastic fibroblasts. There were numerous mitotic figures, many of which were atypical. A small amount of rather poorly vascular stroma was present. The capsule was sharply limited and along at least three-fourths of its circumference was covered with stratified squamous to transitional epithelium. The diagnosis of rapidly growing fibrosarcoma was confirmed.*

Since the tumor apparently was entirely removed it was decided not to risk pulmonary fibrosis by the administration of x-ray therapy. The patient was therefore discharged from the hospital and one month later readmitted for further bronchoscopic study. There was little change in the appearance of the tracheobronchial tree from the previous examinations.

Follow-up study was carried out on the patient during the ensuing four years and repeated x-ray examinations of the chest were made. The last roentgenogram in July, 1948, was again reported within normal limits and she has continued to be well.

SUMMARY

The case of a young girl who expectorated a rapidly growing fibrosarcoma and made an uneventful recovery is reported. Follow-up of the case over a period of over four years has failed to reveal any recurrence. The importance of a microscopic examination of coughed-up material is re-emphasized.

*Drs. Charles Branch and Frederic Parker of the Mallory Institute of Pathology.

A FOREGUT CYST OF THE MEDIASTINUM

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THE finding of alimentary and respiratory tract elements in intrathoracic cysts continues to be an interesting but rare medical and pathologic discovery. A survey of the literature [2, 10, 14, 16, 18, 21, 34] reveals that probably less than ten cases of cysts containing esophageal, gastric, or enteric and respiratory elements have been reported in the literature.[6, 24] It is because of the infrequent occurrence as well as the particular pathologic character of the specimen herein described that the following case is being reported.

Case Report.—The patient, a 24-year-old white man, was admitted to this hospital on Aug. 12, 1947. In 1942 a routine x-ray picture of the chest taken for admission to West Point revealed a mediastinal tumor mass projecting to the right. He was sent to an Army General Hospital where deep roentgen therapy was given with no change in the appearance of the lesion. He was discharged from the service in 1943 because of the mediastinal shadow visualized by x-ray. He was followed by repeated x-ray examinations at this and other hospitals with no demonstrable change in the size or character of the shadow.

At the time of admission the patient had no complaints referable to the chest; he did not appear ill and physical examination revealed no abnormal findings. The past history, family history, and occupational history were noncontributory to the diagnosis. The laboratory findings were not significant.

On Aug. 20, 1947, bronchoscopy was performed. This showed a subcarinal widening with elevation of the right bronchus which was thought to be due to a mediastinal tumor.

On Aug. 26, 1947, under endotracheal cyclopropane, ether and oxygen anesthesia, a right thoracotomy was performed* through a posterolateral incision, utilizing an intercostal approach to the pleural space. A reddish-brown cystic mass was found posterior to the lung, and protruding from the right mediastinum just inferior to the azygos vein. The mediastinal pleura overlying the cyst was incised and dissected from the cyst wall, and the azygos vein was divided and ligated for better exposure. The cyst was dissected from its mediastinal bed. There was no apparent stalk nor connection to the trachea, bronchus, or esophagus. However, it was firmly adherent to the vertebral bodies and to dense tissue which extended to the left of the spine. Although no large vessels were encountered in freeing the cyst, there was moderate bleeding after dissecting the cyst from the vertebral bodies. Hemostasis was secured and the mediastinal pleura was closed with interrupted cotton sutures. The lung was re-inflated and the chest wound was closed in layers with interrupted cotton sutures.

The patient's postoperative course was uneventful and he was discharged from the hospital on the eighth postoperative day to continue his university studies. Follow-up examination and roentgenograms have revealed a normal chest.

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*By Dr. Forrester Raine.

Pathologic Examination.—

Gross description: The specimen (Fig. 1) consisted of a cyst measuring 5.5 by 3.5 cm. after formalin fixation. The cyst wall averaged 2.0 to 4.0 cm. in thickness. The inner surface was corrugated and grayish-yellow and coated by a thick viscid mucous fluid. Section through the wall showed a mucosal, a muscular, and an outer layer.

Microscopic description: The wall of the cyst contained the inner two layers of intestinal tract wall. There was a distinct mucosa, with submucosa, an inner and outer muscular coat, and an adventitial fibrous layer. The primary sections which were cut revealed a gastric type of epithelium lining the mucosa. However, after multiple sections were cut from different areas of the cyst wall, three types of epithelium could be identified. In some areas esophageal mucosa comprised of noncornifying squamous-cell epithelium was seen which merged into a respiratory epithelium consisting of ciliated, goblet cells. In other areas there was a poorly defined mucosa which was taller than the other two. The cells were poorly outlined, but seemed to have the appearance of stratified mucous glands such as might be seen in the stomach (Fig. 2, *A*, and *B*). In the submucosa there were collec-

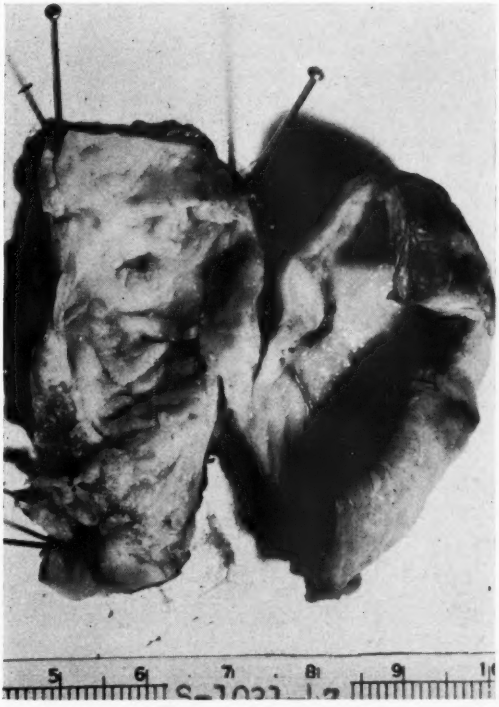
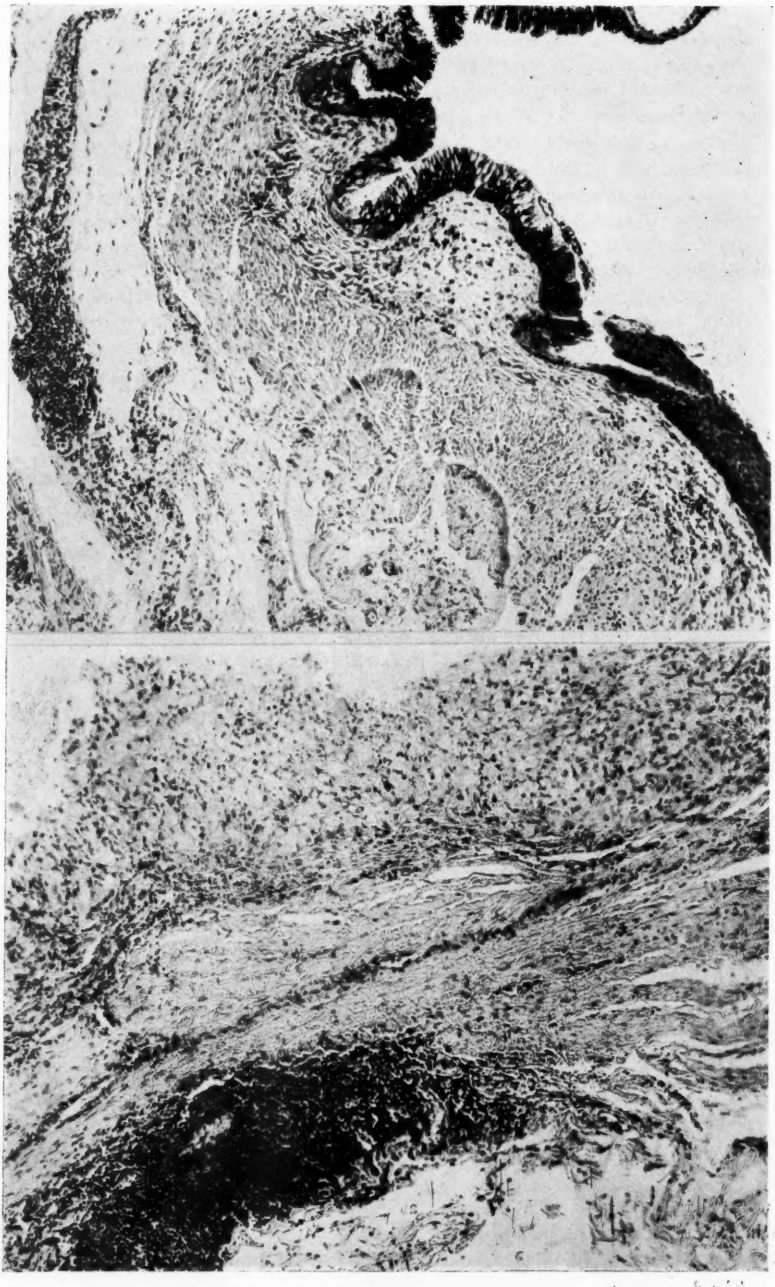


Fig. 1.—Gross specimen of foregut cyst showing mucosal lining.

tions of lymphocytes in both follicular and diffuse formation. The musculature showed distinct circular and longitudinal muscle bundles. The outer layer contained fibrous tissue and blood vessels.

The diagnosis was foregut cyst of the mediastinum.

A.



B

Fig. 2.—*A*, Photomicrograph (low power) showing transition between esophageal and bronchial epithelium; smooth muscle is seen below the mucosa. *B*, Epithelial lining resembling degenerated gastric mucosa.

DISCUSSION

The origin of these cysts has long been a subject of speculation by numerous investigators. Their occurrence primarily in children and the resemblance of the epithelial elements to embryonic prototypes have caused most workers interested in the subject to turn to embryologic maldevelopment as a probable explanation of their genesis. There have been many theories advanced attempting to explain these anomalies. These concepts have been:

1. Origin from embryonic diverticula of the alimentary system or foregut. This hypothesis is considered most likely by the majority of authors.
2. Origin from vestigial remnants of the omphalomesenteric system or vitelline duct.
3. Failure of coalescence of the vacuoles in the transverse axis when the alimentary tube is in the solid stage. Thus, a cystic structure is left contiguous to some portion of the alimentary tract.
4. Sequestration of embryonic multipotential entodermal cells from the lung bud area of the primitive alimentary anlage, with later growth and development.
5. Imbalance of organizational substances in embryonic life.
6. Abnormal or isolating twinning theory of origin similar to dermoids and teratomas.

It is clear that no single theory of origin has been found completely acceptable for mediastinal cysts,[27] and various pathologic processes, including metaplasia and neoplasia, have been invoked to explain the two different histologic findings that have been described.

The histologic pattern of the cyst in our case presents an epithelium from both the alimentary and bronchial systems. The primitive foregut has potentialities of developing into both respiratory and enteric epithelium. During the fourth week of development of the embryo, lung buds develop as an evagination from the esophagus. At this embryonic stage the pinching off of an outbud or diverticulum of foregut could be carried along by the downward growing lung bud and lodge in the mediastinum or it may remain attached to its esophageal origin. We are, therefore, in accord with those writers who ascribe these anomalies to diverticula of the embryonic foregut.

The histologic character and differentiation of the various mediastinal cysts has been adequately described by a number of authors.[2, 3, 13, 18, 19] In describing the bronchiogenic cysts, most writers have considered not only the characteristic epithelium, but have stressed the finding of cartilage in the wall of the cyst. The comparative incidence of bronchiogenic cysts was illustrated by the series of ninety-four cases of benign mediastinal tumors reported by Blades,[2] in which twenty-three of the tumors were bronchiogenic cysts and twenty were teratoid types. It is possible that a definite classification of these

cysts may be impossible, due to complete destruction or dissolution of the lining, as was found in the case reported by Donald.[8] In reviewing, we attempted to evaluate the effect of the roentgen therapy which the patient has received upon the pathologic findings, but we are unable to demonstrate any definitive features that we could ascribe to the radiation.

In the specimen described, the most interesting pathologic feature was the varied and transitional character of the epithelium, which was seen in the mucosa. A combination of the respiratory or ciliated columnar epithelium and the alimentary or stratified squamous and mucous gland type of mucosa has been reported previously,[24, 29, 32] but it has not been frequently described in the literature. It would, perhaps, be more commonly seen if many sections were examined from the so-called bronchial or gastric cysts, or esophageal duplications.

The asymptomatic nature of the case reported has been a finding rather commonly reported by others and indicates nonfunction of the mucosal elements.[2, 14, 28, 31, 32] The fact that these cysts, however, may frequently cause symptoms and lead to a variety of complications has been stressed by a large number of workers. The common symptoms that have been described in association with mediastinal cysts of this type have been cough, dyspnea, cyanosis, hemoptysis, pleuritic pains, recurrent bouts of pneumonia, dysphagia, fever, and malaise. Most of the complications arising from the cysts that have been described were found to occur in children. These have consisted of rupture into a bronchus, pleural space, or the trachea, often due to perforation of a peptic ulcer arising from gastric mucosa,[1, 6, 7, 26] erosion of the vertebra or ribs or erosion of the esophagus, and, secondarily, they have been the cause of atelectasis, pneumonitis, empyema, and bronchiectasis.[7] Many other anomalies that were usually developmental in nature have been described in association with these lesions and the cysts have also been described as extending down to and below the diaphragm into the stomach.[7, 32]

The treatment of choice of the posterior mediastinal cyst is undoubtedly exterpation in a one-stage procedure if this is possible. Heuer and Andrus[14] have stressed the danger of neglecting these lesions, and the importance of operation both from a diagnostic and therapeutic standpoint. These authors have further emphasized the hazard and futility of subjecting their patients to preoperative irradiation because of the lack of therapeutic response and the fibrous reaction resulting from this procedure. The risk of the operation has lessened in the past two decades to a point that the danger of thoracotomy is not as great as the risk created by the presence of the tumor.

The procedure used in this patient illustrates the type of operative approach we prefer in lesions of the posterior mediastinum. We have felt that the posterolateral incision with or without the removal of a rib has given adequate exposure to this region and the postoperative recovery has been excellent in these patients.

SUMMARY

1. A foregut type of posterior mediastinal cyst occuring in a 24-year-old white man is presented.

2. The pathologic examination of the cyst revealed a lining epithelium similar to that found in the respiratory tract, esophagus, stomach, and intestines.

3. The cyst was removed in a one-stage operation through a posterolateral approach with complete recovery.

The authors are indebted to Mr. Leo Massopust, Marquette University School of Medicine for the Photomicrographs and to Dr. Joseph M. Lubitz, Pathologist, Veterans Hospital, Wood, Wis., and Marquette University School of Medicine, for his valuable assistance in the preparation of this report.

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THE TREATMENT OF SIMPLE SPONTANEOUS PNEUMOTHORAX

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SIMPLE spontaneous pneumothorax is a well-defined clinical syndrome exhibiting the following characteristics: The pneumothorax occurs spontaneously (in contradistinction to artificial or traumatic pneumothorax) and not as a complication of any other marked diseases (inflammatory or tumorous) of the lung, trachea, esophagus, or the thoracic wall, and, finally, the disease is not accompanied by secondary infection.

The etiology may vary, a point which it is of the utmost importance to bear in mind when working out the method of treatment. The commonest cause seems to be spontaneous rupture of subpleural valvular cysts. Evidence to this effect was first presented in this country by Kjaergaard (1932) on the basis of nine autopsy findings (six cases reported in the literature, three cases personally observed). The author describes two different types. In one type the valve is formed by emphysematous tissue, in the other by scar tissue. An additional two cases are reported in a later publication. In either case autopsy revealed multiple congenital cysts. In one case the cysts communicated with the pleural cavity through a small aperture. The observations of Kjaergaard have been confirmed by numerous other authors (Gordon; Grapengiesser; Sycamore; Castex and Mazzei; Mourier; Gullbring and others). On the basis of studies of familial cases the possibility was suggested that congenital defects in the pulmonary tissue may be a contributing cause of the formation of subpleural vesicles with ensuing pneumothorax (Götzsche; Orrego Puelme and Richard).

Cutler reports cases of spontaneous pneumothorax which occurred in the course of artificial pneumothorax therapy and were cured after cauterization of adhesions. He is, therefore, of the opinion that the causative factor may be small fissures in the visceral pleura brought about by the traction of adhesions. As regards our Case 2 this explanation seems obvious.

Based on anatomical, clinical, and experimental studies Macklin advanced the theory that pneumothorax may develop in consequence of a small fissure in the mediastinal pleura which in the presence of interstitial emphysema may be exposed to overdistention and may burst.

The mechanical factor responsible for the rupture of vesicles is assumed to be the increased pressure which occurs under forced expiration in the presence of a valvular system (Macklin).

The symptoms and the objective manifestations of the disease are well-known and we shall confine ourselves to re-emphasizing that to some extent the symptoms are proportional to the suddenness at which the air enters the pleural cavity and the actual amount of air involved. In some cases the symptoms are hardly evident, or absent. Roentgenographic examination, however, makes it possible to disclose the presence of even quite small quantities of air, which are

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distinctly observable under forced expiration. In some cases roentgenography has furthermore made it possible to detect subpleural vesicles or cysts (Kjaergaard; Gordon; Sycamore; Castex and Mazzei). By this means cysts were revealed in two of the cases studied by us (Cases 5 and 8).

Roentgenographic examination is usually an insufficient means of detecting minor cysts which do not show up owing to their small size, their location or the thinness of the cyst wall. In the more recent literature a few authors have mentioned thoracoscopy as a valuable aid in detecting the presence of vesicles (Sycamore; Castex and Mazzei; Mourier; Gullbring; Begtrup-Hansen; Brock).

Routine thoracoscopic examination was carried out in all our cases except two in which roentgenography revealed the presence of cysts.

In case of complete pneumothorax where the location of the process is usually unknown it is advisable to insert the thoracoscope in the fifth or sixth intercostal space in the posterior axillary line or in the midaxillary, from where one will obtain an excellent view of the surface of the lung. The picture presenting itself is most characteristic and cannot possibly be mistaken for any other lesion of this area, as it will reveal a smaller or larger number of thin-walled transparent emphysematous blebs of varying size localized within a more or less extensive area. Sometimes a fistula is seen (Case 6), but it will generally be closed owing to the collapse of the lung. One cannot in all instances expect to obtain a complete view of the extent of the process, as it is not always possible to look into the fissures and the mediastinal surface. Thus, in Cases 4 and 7 the process appeared to be far more extensive than revealed by thoracoscopy. The fact that it is impossible to view the entire pleura and thus ascertain the extent of the process will undoubtedly necessitate exploratory thoracotomy in some cases (frequently recurring pneumothorax, chronic pneumothorax) even though thoracoscopic examination is negative.

Considering the results obtained in cases reported in the literature and in our own material and in view of the minimum risk involved by thoracoscopy, the institution of routine thoracoscopic examination is recommended in cases of spontaneous pneumothorax.

The prognosis of spontaneous pneumothorax is generally regarded as favorable with a tendency to spontaneous resorption of the air and re-expansion of the lung within a few weeks, but the increased number of cases observed and the prolonged period of observation have afforded knowledge of the serious complications which may occur in the course of the disease, and it is, therefore, no longer justifiable to regard the disease as absolutely benign.

The most frequent complication is the recurrence of attacks. Cohen and Kinsman observed recurrence of symptoms in 10 per cent, Wilson in 20 per cent, Kjaergaard in 15 per cent, Ornstein and Lercher in 30 per cent, Wood in 45 per cent and Schneider and Reissman in 20 per cent of the cases studied by them. In our material recurrence was observed in five cases of eight. The number of recurrent attacks is greatly varying, from one or two (as seen in the majority of cases) to numerous. Thus, Locke reports a case of eighteen recurrent attacks. Also the intervals vary greatly. It is obvious that the patient may

be troubled by recurrent attacks for a number of years. In recurrent attacks the symptoms are frequently mild or indefinable and are sometimes only manifested by slight functional dyspnea which makes it difficult to establish a correct diagnosis (Schneider and Reissman). It is, therefore, likely that the incidence is higher than generally assumed.

In other cases the spontaneous pneumothorax becomes chronic, for example, when traction of adhesions prevents healing of the fissure (Kjaergaard; Hoyer and Clagett; Mainini and Alvarez; Babington; Schoner and Erlich). In the presence of fairly large accumulations of air this may give rise to a permanent feeling of oppression of the chest and dyspnea. The patients are frequently weak and miserable and are progressively losing weight which makes them look like hunger patients (Brock).

The presence of a valvular system always involves the risk of the patient's developing tension pneumothorax, always a serious condition which, if untreated, may result in death. Kjaergaard observed this complaint in 10 per cent of his cases, Movitt in 16 per cent. Cases of bilateral tension pneumothorax are reported by Wood and by Emerson and Beeler.

Finally, there are occasional occurrences of pneumothorax complicated by hemothorax; Kjaergaard reports two cases out of fifty-one.

The fact that Kjaergaard, in reviewing the literature, found that death was reported in six cases out of 200, serves to prove that the mortality rate is not quite negligible. In his own material there are no cases in which death may be attributed entirely to the existing pneumothorax, but in two cases the pneumothorax was complicated by other lesions of the lungs and may safely be regarded as a contributing cause. In one case the patient developed pneumonia of the collapsed lung and, subsequently, pyopneumothorax; in the other case a left-sided tuberculosis was treated with artificial pneumothorax when the occurrence of a right-sided spontaneous pneumothorax resulted in death.

TREATMENT

As the ordinary conservative therapy consisting of complete rest in bed for some weeks and, in cases of mediastinal displacement and tension pneumothorax, exsufflation, often proves to be insufficient even as the initiation of more radical treatment, we shall give an outline of the method by which these patients should be treated in the acute stage of illness.

When the diagnosis has been established intrathoracic pressure should be measured. If the pressure is elevated, aspiration should be resorted to until the manometer registers zero. Aspiration is likewise indicated in cases where the lung is totally collapsed, even though there is no elevation of the pressure. The patients should now be kept under constant observation and it may be necessary to carry out repeated aspirations or, even better, to insert a drainage tube (Bülau drainage) ending under water or connected with a permanent suction device. The drainage tube should preferably be inserted in the second or third intercostal space anteriorly. The application of drainage averts the danger of disastrous conditions occurring and further treatment may be considered.

Knowledge of the above-mentioned quite frequent complications made some authors advocate a more active therapy. They aimed at complete agglutination of the two pleural membranes which was attained through the production of chemical pleuritis by means of irritant substances. Hypertonic solution of glucose, blood and iodine talcum were applied for this purpose (Hemmel; Bethune; Kulke; Singer and associates; Watson and Robertson). According to Movitt and associates hypertonic glucose is of doubtful value as, in some cases, it gives rise to great exudate but no adhesions. Injection with blood may lead to the formation of fibrin clots preventing re-expansion of the lung. Iodine talcum and similar kinds of powder produce severe pleuritis with marked thickening of the pleura which becomes liable to contract, another factor preventing re-expansion of the lung. In patients treated by this method autopsy findings revealed thickenings of 1 cm. (reported by Ross and Fullerton).

The application of silver nitrate yielded more favorable results. This method was introduced by Brock in 1932. While the patient is lying on the back about 0.5 to 1 c.c. of silver nitrate in 10 per cent solution is injected into the third intercostal space and at the same time exsufflation is carried out. During the first two or three days there is an accumulation of fluid which is aspirated. Fever and pain persist for four or five days. The pleura is said to become dry within ten to fourteen days. By this method Brock treated eighteen patients, twelve with chronic pneumothorax, six with recurring pneumothorax. Complete recovery is reported in all cases. Frequently injections had to be administered two or three times.

THE AUTHORS' MATERIAL

For the past two years we have treated eight cases of simple spontaneous pneumothorax in the Department of Thoracic Surgery of the Rigshospital. In seven of these cases subpleural vesicles or pulmonary cysts were detected, and in one case a small aperture of a fistula was observed immediately beneath an adhesion. In two cases only did roentgenographic examination reveal the presence of cysts, in the remaining cases it was necessary to carry out thoracoscopy in order to be able to establish a correct diagnosis. Of these eight patients four were women aged 20, 21, 26, and 30 years, respectively, and four were men aged 24, 29, 42 and 55 years, respectively. In all these cases the cysts were located in the upper lobe particularly in the lower portion of the anterior margin. There were five instances of left-sided involvement, three instances of right-sided involvement. Three cases were treated with silver nitrate and in five cases pulmonary resection was carried out.

TREATMENT WITH INJECTION OF SILVER NITRATE (THREE CASES)

In three cases we used the method of Brock, slightly modified. When the lesion had been localized by means of thoracoscopy we inserted a long cannula into the thoracoscope and injected 0.5 to 1 c.c. of silver nitrate in 10 per cent solution into the surface of the lung corresponding to the location of the lesion. This part of the procedure is most painful and is carried out under general anesthesia.

CASE 1.—E. H., a man, aged 42 years, had previously been in good health.

On June 9, 1946, he suddenly experienced heavy pain in the left side of the chest with great dyspnea and had to go to bed. The roentgenographic examination which was carried out a couple of days later disclosed complete collapse of the entire left lung. Four months later complete re-expansion of the lung was observed. On Jan. 11, 1947, the patient experienced a similar attack while starting a motorcar, also this time the attack was accompanied by great dyspnea. On January 13, roentgenographic examination revealed a great left-sided pneumothorax with displacement of the heart and mediastinum toward the right. On January 14, thoracoscopy was carried out. Small emphysematous blebs were observed in the anteroinferior portion of the upper lobe, near the fissure. About 1 c.c. of silver nitrate in 10 per cent solution was sprinkled onto this location. On follow-up examination in July, 1947, the patient had recovered completely. Roentgenography showed complete re-expansion of the lung and there was no evidence of exudate or thickening of the pleura.

CASE 2.—J. J., a man, aged 24 years, was admitted to the hospital on April 4 and discharged on April 25, 1947.

He had been hospitalized elsewhere twice in 1944 and once in 1945 for spontaneous pneumothorax. He received conservative treatment. The onset was sudden and could not particularly be ascribed to exertion. The attacks were accompanied by violent pain in the right side of the chest, radiating into the arm, and the patient was suffering from dyspnea and a dry cough. No previous manifestations of tuberculosis had been noted.

On April 3, 1947, the patient experienced a recurrent attack in consequence of which he was admitted to this hospital. Roentgenographic examination revealed a large right-sided pneumothorax with no displacement or exudate. On April 8, thoracoscopy was carried out. No cysts or blebs were seen, but on the other hand a wide adhesion extending from the apex to the top of the cupola was observed. Beneath this adhesion there was a minor cavitation containing a small amount of serosanguineous fluid. On the assumption that this had been the site of a small ruptured bleb about 1 c.c. of silver nitrate in 10 per cent solution was injected onto this location.

A roentgenographic check on April 15 revealed almost complete re-expansion of the lung.

On May 5, 1948, however, a large pneumothorax was once more observed, wherefore exsufflation was carried out.

On follow-up examination on May 28 the patient was feeling well and complete re-expansion of the lung was observed.

CASE 3 (Figs. 1 and 2).—E. L., a man, aged 55 years, was admitted to hospital on June 10 and discharged on July 22, 1947.

During a coughing fit in November, 1946, the patient suddenly experienced violent pain in the right side of the chest, accompanied by great dyspnea. The attending physician ascertained the presence of a right-sided pneumothorax; roentgenographic examination was not done. In the following days repeated aspirations were carried out and after one month in bed the patient was feeling quite well. In May, 1947, he experienced another attack of exactly the same nature and was admitted to the hospital. Roentgenographic examination revealed a total right-sided pneumothorax with displacement of the mediastinum.

On June 10 the patient was admitted to the Rigshospital. He was lean, weak, and anoretic. Thoracoscopic examination the following day revealed collapse but no atelectasis of the lower and middle lobes. Numerous wide adhesions were seen over the upper lobe which obscured the view considerably, but no cysts or fistulas were seen. About 1 c.c. of silver nitrate in 10 per cent solution was injected, a drainage tube was inserted into the cavity and permanent suction applied.

The following days the temperature ranged between 38.5 and 40° C. Roentgenographic examination on June 16 showed that a large pneumothorax persisted in the upper part of the lung. Thoracoscopy was therefore repeated on June 17, this time high in the axillary region. The lower part of the lung had become re-expanded, but in the upper part a cavity

with numerous adhesions persisted. A second injection of about 1 c.c. of silver nitrate in 10 per cent solution was administered and another drainage tube was inserted into the top of the axillary.

As there was a persistent rise of temperature, penicillin and sulphathiazole were administered as from June 26, whereupon the temperature dropped to normal. A roentgenographic check on August 8 revealed a fairly large exudate but no pneumothorax.

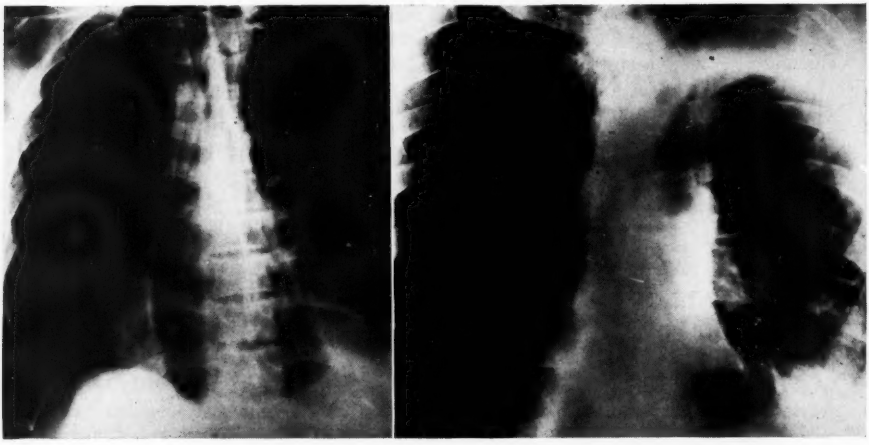

Fig. 1. Fig. 2.

Figs. 1 and 2 (Case 3).—Roentgenograms immediately before and eight months after silver nitrate therapy. Fig. 1 reveals a pneumothorax in the upper part of the right lung with displacement of the trachea toward the left. Fig. 2. The roentgenogram shows an organized exudate over the apex of the lung with displacement of the trachea towards the right.

Silver nitrate therapy yielded most satisfactory results in two of the three cases so treated, whereas in the third case there was an organized exudate with displacement of the trachea. There is frequently a violent response to the injection in the form of fever which may persist for several weeks. The treatment is always painful and in our opinion it is more disagreeable than the operative method.

Even though results are satisfactory in most cases this is, however, only a symptomatic method of treatment which does not remove the causative factor in the lung. The drawbacks of the methods of producing chemical pleuritis may be summarized as follows: (1) incomplete re-expansion, (2) frequently severe pleural changes and, finally, (3) a combination of the two.

The latter drawback is, we presume, not quite unusual and may lead to development of chronic pneumothorax which will be resistant to any form of treatment by more conservative methods. A case of this nature will be described in the following. Since the patient received primary treatment in another hospital the case is not included in our material.

CASE HISTORY.—A. A., a girl aged 12 years, was admitted to the hospital on April 29 and discharged on May 17, 1947.

On May 18, 1945, while on a bicycle trip the patient suddenly became affected with great dyspnea accompanied by indefinable pain in the chest. The attack subsided spontaneously in the course of a few hours. A fortnight later the patient experienced a similar

attack because of which she was admitted to a hospital elsewhere. A large left-sided pneumothorax was observed with displacement of the heart and mediastinum. Numerous aspirations proved ineffectual.

On Aug. 20, 1945, thoracoscopy revealed collapse of the lung but no atelectasis. The upper lobe and the upper part of the lower lobe communicated medially with the thoracic wall through numerous wide adhesions. No fistula aperture was seen, but at the base of one adhesion there was a small emphysematous bulla. Following cauterization of the adhesion the lung appeared to be detached.

Roentgenographic examination on November 6 revealed complete re-expansion of the lung.

The patient was now doing well until May 28, 1946, when the presence of a large pneumothorax was once more detected. 2.5 c.c. of silver nitrate in 10 per cent solution was injected under ethyl chloride anesthesia. In the following days repeated aspirations were carried out. On the twelfth day 150 c.c. of brownish serous liquid was aspirated. Despite repeated subsequent aspirations a pneumothorax persisted over the upper part of the lung.

On April 29 the patient was admitted to the Department of Thoracic Surgery of the Rigshospital, where it was assumed that pleural changes were responsible for the failure of the lung to re-expand.

On May 1 thoracotomy with decortication of the lung was carried out. A fairly large pneumothorax was pushing the upper lobe and the upper part of the lower lobe downward. Either lobe was covered by pleural thickenings preventing re-expansion of the lung. No fistulas or vesicles were seen. The lung was dissected free all the way round and excision of the inferior ligamentum pulmonale was performed. Subsequently the lung became more mobile but failed to become completely re-expanded; the thickened pleura over the upper and lower lobes was therefore removed. A drainage tube was inserted.

Roentgenographic examination carried out on May 4 showed a fairly large pneumothorax. The pleural cavity was punctured and about 75 c.c. of serosanguinolent fluid and some air were evacuated.

On May 10 the drainage stopped functioning whereupon a Bülau drainage tube was inserted. Now the lung re-expanded, but on May 17 when the patient was discharged a small pneumothorax persisted. This was subsequently replaced by a localized exudate which was evacuated.

Roentgenographic examination carried out in December, 1947, revealed increased exudate. Pleural puncture showed that the chief portion was organized, it being possible to evacuate only a few c.c. of hemorrhagic fluid.

Other methods of treatment have been attempted, but like the production of chemical pleuritis these methods seem quite insufficient from a surgical point of view. Electrocoagulation of the aperture of the fistula might produce healing in some cases but will not remove the cause of the disease (This method of treatment was applied unsuccessfully in our Case 6). The same holds good of scarification of the pleura (Churchill) and simple suture of the fistula (Movitt and associates) either of which requires fairly extensive thoracotomy.

PULMONARY RESECTION IN THE TREATMENT OF SPONTANEOUS PNEUMOTHORAX (FIVE CASES)

The development of thoracic surgery has made a more radical therapy possible. Thus, Tyson and Crandal as well as Hoyer and Clagett have successfully performed resection of pulmonary cysts in spontaneous pneumothorax. In our material pulmonary resection was performed in five cases with beneficial results.

CASE 4 (Figs. 3 and 4).—K. N., a girl, aged 21 years, was admitted to the hospital on Dec. 12, 1946 and discharged on Jan. 11, 1947.

In August, 1947, for unknown reasons, the patient suddenly experienced violent pain in the left side of the chest accompanied by dyspnea. Conservative treatment for six weeks proved ineffectual. Since then great functional dyspnea persisted and the patient was, therefore, admitted to the Department of Thoracic Surgery of the Rigshospital on December 12.

Roentgenographic examination revealed total left-sided pneumothorax with no displacement of the mediastinum. Thoracoscopy showed an emphysematous bleb about the size of a grape in the lingular area—no other abnormalities were observed.

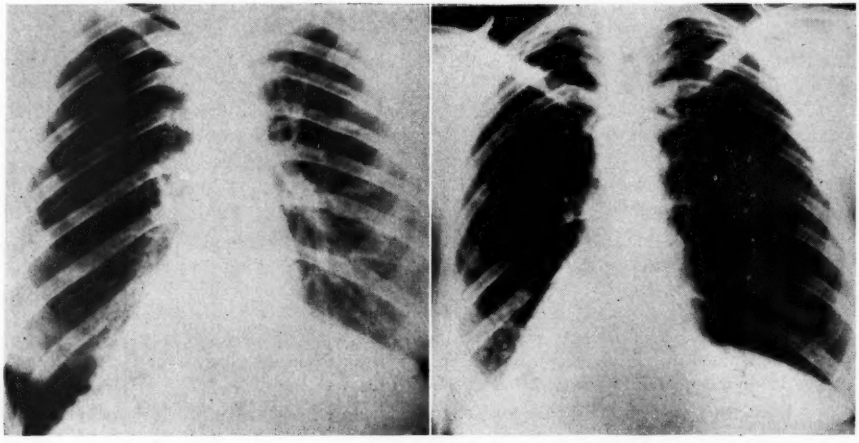

Fig. 3. Fig. 4.

Figs. 3 and 4 (Case 4).—Roentgenograms obtained immediately before and twelve months after pulmonary resection. In Fig. 3 a moderately great left-sided pneumothorax is seen. Fig. 4: 12 months postoperatively the roentgenogram reveals complete re-expansion of the lung with distinct pleural coverings in the sinus phrenico-costalis. There is evidence of partial regeneration of the removed rib.

On Dec. 27, 1946, thoracotomy was carried out with resection of the affected area which proved to be more extensive than revealed by thoracoscopy. Postoperative course was uneventful.

On follow-up examination on Jan. 24, 1948, the patient was in good health. Roentgenography showed slight basal pleural opacity, otherwise no abnormalities.

CASE 5.—E. H. P., a girl, aged 29 years, was admitted to the hospital on June 4 and discharged on July 5, 1947.

In 1941 she had left-sided pleuritis. In 1942, she had an appendectomy complicated by pneumonia. Otherwise there was no history of previous disease.

While walking against the wind, in October, 1944, the patient suddenly experienced violent pain in the chest accompanied by great dyspnea. The patient was admitted to a hospital elsewhere and a diagnosis of great left-sided pneumothorax was established. From this date up to the date of admission the patient experienced five similar attacks.

On May 11, 1947, the patient experienced a recurrent attack of the usual nature and was admitted to the Department of Thoracic Surgery of the Rigshospital on June 4. Daily aspiration of about 500 c.c. of air was ineffectual. Subsequent roentgenographic examination revealed a cyst in the upper lobe about the size of a walnut.

On June 12 thoracotomy was performed. Three cysts were observed, one about the size of a walnut and two smaller ones at the top of the apex. Some adhesions extending

from the cyst to the thoracic wall were cut and the affected area resected. Postoperative course was uneventful.

On follow-up examination on August 11 the patient was found to be in good health. Roentgenography showed complete re-expansion of the lung.

CASE 6.—K. L., a girl aged 20 years, had from childhood a tendency to become dyspneic.

Roentgenographic examination carried out nine months prior to hospitalization revealed no abnormalities. (A subsequent check of the x-ray plates, however, disclosed a small cyst in the upper lobe.) Six months prior to hospitalization the patient suddenly experienced slight pain in the right side of the chest. At that time the presence of a moderately large pneumothorax was discovered.

At the time of hospitalization the patient suffered from slight dyspnea, otherwise no particular symptoms. Roentgenographic examination revealed a small pneumothorax in the upper part of the lung, whereas the lower part was found to be adherent to the thoracic wall.

On August 21 thoracoscopic examination revealed the presence of a large pulmonary cyst in the right upper lobe. At the top of the cyst there was a small aperture the surroundings of which were electrocoagulated. The smoke resulting from this was blown in and out through the hole. A drainage tube ending under water was inserted.

In the following days the temperature rose from 40 to 41° C. Following penicillin therapy the temperature gradually returned to normal, but as the pneumothorax persisted, thoracotomy was performed on September 9, with resection of the cyst which was adherent to the thoracic wall through cordlike adhesions. The detached part of the cyst was removed. A small bronchus was seen at the bottom. The side walls were electrocoagulated and sutured.

On follow-up examination twelve months later there were no complaints. Roentgenography showed small pleural coatings over the apex and the diaphragm, otherwise no abnormalities.

CASE 7.—I. H., a woman aged 30 years, was admitted to the hospital on Dec. 5, 1947, and discharged on Dec. 22, 1947.

Some day in June, 1947, the patient suddenly experienced heavy pain in the left side of the chest accompanied by great dyspnea. She was admitted to a hospital elsewhere. Here the patient was found to be affected with a total left-sided pneumothorax with displacement of the heart and mediastinum. Following repeated aspirations the patient became symptom free.

Two weeks prior to admission to the Rigshospital the patient experienced a recurrent attack of the same nature. At the time of hospitalization the patient was suffering from slight dyspnea. Roentgenographic examination revealed a total pneumothorax with a small exudate in the sinus.

Thoracoscopy was carried out on December 8. A thin-walled emphysematous bleb about the size of a cherry was observed in the upper lobe anteromedially. The lower lobe was atelectatic.

On December 12 thoracotomy with resection of the affected area was performed. In this location there was a cyst having a pedicle about 2 cm. wide. A number of cordlike adhesions extended from the cyst to the thoracic wall. The cyst was resected.

The portion removed was easily reinflated through a small bronchus and now another small cyst became visible on one side of the inflated vesicle. In this cyst there was a small slit which was closed by a clamp. Thereupon it was possible to inflate also this cyst through another small bronchus. It was impossible to reexpel the air by pressure of the fingers. There is, therefore, no doubt that in this case there existed a valvular system in which the valvular vesicle ruptured. On follow-up examination on Jan. 7, 1948, the patient stated that she was in good health. Roentgenographic examination revealed complete re-expansion of the lung.

CASE 8.—C. G. H., a man aged 39 years, was admitted to the hospital on Dec. 31, 1947, and discharged on Jan. 16, 1948.

On Dec. 20, 1947, while working, the patient suddenly experienced violent, shooting pain in the middle of the thorax and the abdomen, accompanied by heavy dyspnea and cough. The physician first attending the patient regarded the case as a lesion of the abdominal rectus. The patient was referred to the surgical polyclinic of the Rigshospital where the presence of a large pneumothorax was detected and the patient was hospitalized.

Roentgenographic examination revealed total right-sided pneumothorax with no displacement of the mediastinum. In the upper lobe a net like shadow was distinctly observable which suggested the presence of cysts in this location. Thoracoscopy was not carried out owing to the positive roentgenographic findings. On Jan. 2, 1948, thoracotomy was performed with lobectomy of the right upper lobe. Superoposteriorly in the upper lobe an area the size of an orange was seen covered with numerous vesicles of varying size; anteriorly there was an area containing minute densely grouped cysts. Along the lower boundary there was a string of fine emphysematous blisters resembling tiny beads. Segmentary resection was first attempted, but had to be given up, wherefore lobectomy was carried out. A drainage tube with permanent suction was inserted.

Roentgenographic examination carried out on January 6 revealed a small pneumothorax over the apex with reflecting liquid. Following pleural puncture 25 c.c. of clear liquid and 60 c.c. of air were withdrawn.

On follow-up examination on February 9, the patient was feeling well, Roentgenographic examination revealed that a small pneumothorax, about the same size as detected by examination on January 12, persisted over the apex.

Our experience with operative treatment of the disease has been favorable, the follow-up examinations having shown subjective well-being of the patients and the roentgenological changes having been only slight. As a rule we observed only obliteration of the sinus angle or small localized coatings of the pleura. In one case a small pneumothorax persisted one month after the operation, but from experience gained in other lobectomies it is safe to assume that spontaneous resorption will take place.

Surgical intervention was indicated by chronicity in two cases (Cases 4 and 6), by recurrence of attacks in two cases (Cases 5 and 7). In one case roentgenographic examination revealed the presence of cysts and was thus suggestive of an extensive process (Case 8). It is our impression that the patients receiving operative treatment do not have to stay in bed for so long a period as those receiving silver nitrate injections. The five patients operated on by us left the hospital on the thirteenth, fourteenth, fifteenth, twenty-third, and thirty-third postoperative days, respectively. In the last case special circumstances prevailed. Patients receiving conservative treatment exclusively frequently have to stay in the hospital or in a sanatorium for several months.

CONCLUSION

The present status of thoracic surgery makes it possible at practically no risk to undertake radical treatment of spontaneous pneumothorax aiming at complete extirpation of the affected area. Such treatment is especially indicated in cases where chronicity develops or where recurrent attacks or tension pneumothorax occurs.

While medical treatment, naturally, does not remove the actual cause of simple spontaneous pneumothorax, that is, the cysts or the vesicles, roentgeno-

graphic and especially thoracoscopic examination are valuable aids in establishing a correct diagnosis and locating the process which, in turn, makes surgical treatment possible.

Experience confirming the theoretical views shows that the safest surgical treatment is complete resection of the affected area. The other more conservative methods, such as the production of chemical pleuritis, electrocoagulation, or simple suture of the fistula, do not fulfill the requirements, namely, complete recovery, as they do not preclude the possibility of recurrent attacks.

In cases where it is likely that adhesions will bring about rupture of the visceral pleura resulting in pneumothorax, cauterization of adhesions will undoubtedly constitute sufficient therapy.

SUMMARY

A survey is given of the literature with special reference to etiology and diagnosis. Routine thoracoscopy is recommended as a valuable aid in establishing the correct diagnosis and locating the site of the disease in cases where roentgenographic examination is negative.

In our series of eight patients thoracoscopy was carried out in six cases. In five of these cases cysts were detected in the upper lobe, in one case a presumably ruptured subpleural vesicle was observed at the base of a wide adhesion.

Three of our eight patients received treatment by the method of Brock, 1 c.c. of silver nitrate in 10 per cent solution being injected. In two of these cases results were satisfactory, whereas in one case a fairly great organized exudate was seen over the top of the lung with marked displacement of the trachea.

In five cases resection of the affected area was carried out successfully. One month postoperatively a small pneumothorax over the apex of the lung was observed in one case, the remaining cases revealed no abnormalities apart from insignificant pleural opacity.

The latter method is recommended as being the most rational, whereas the silver nitrate method of Brock should be reserved for debilitated and elderly individuals whom it would not be advisable to expose to major surgery, and for cases of multiple cysts.

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THE ANESTHETIC BLOCKING OF THE VAGUS, THE SYMPATHETIC AND THE PHRENIC AT THE NECK IN THORACIC SURGERY— ITS PROTECTIVE ACTION ON BLOOD PRESSURE

Experimental Researches

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DURING the ten years from 1938 to 1948 a considerable step forward has been made in thoracic surgery, as is witnessed by the large number of operations successfully carried out and duly checked in the process of time, showing the high degree of technical perfection reached by the surgical cure of endothoracic diseases. An important contribution has been offered by the constant improvements in narcosis by hyperpressure, while a further improvement has been obtained through the realization of controlled respiration, enabling the overcoming of respiratory difficulties caused by an opening in the thorax. By way of curarization it is now possible to obtain complete muscular relaxation of the patient, even when using a moderate dose of anesthetic.

Through this particular form of narcosis it is possible to maintain, in all circumstances, an efficient respiratory exchange, even during the eventual opening of both pleural cavities. Thus, while apnea was formerly cause of complications and death, today, with controlled respiration narcosis, it can always be obtained when complete immobilization of the operative field is required. It is, however, advisable during endothoracic interventions on the lung, not to reach a total collapse of the healthy lobes of the lung on the operated side, for a complete collapse, extending for a fairly long time, might prevent re-expansion in the period immediately following operation (Meier). The opening of the thorax nullifies the negative pressure essential to the proper filling of the heart, with the result that a smaller quantity of blood reaches the lung. By using an endotracheal tube which enables the respiratory muscles to be set at rest, this complication may be relieved, but it is impossible to avoid the increase of endopulmonary pressure with its consequent increase of respiratory resistance. Though by controlled respiration and by the use of curare a substantial improvement has been reached, yet hitherto it has been impossible to conquer the numerous nervous reflexes caused by operative maneuvers on endothoracic, mediastinal and hilar tissues, resulting in cardiocirculatory depressions, as was demonstrated even recently by Biancalana, Dei Poli, and Soave in intubated and curarized animals.

The pathogenic mechanism of such phenomena, in which the reflex nature appears certain, had been the object of study by a large number of experimenters. Yet the problem of the presence of cardiocirculatory and respiratory disturbances caused by operative maneuvers on the vagosympathetic plexus remains unsolved.

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In order to give a clearer insight of the problem which I am endeavoring to examine, I shall submit a few remarks on lung innervation.

The vagus nerve of the right hemithorax, after having given rise to the recurrent nerve, gives off the thoracic branches divided into tracheal, bronchial, esophageal, pericardial, and infracardial.

Morin and Dei Poli include among the thoracic branches the "middle cardiac" which they have often noticed arising from the vagus nerve, below the recurrent nerve, while other authors have found these nerves actually to originate from the recurrent nerve.

The anastomosis of the cardial nerves of the vagus with those of the sympathetic-thoracic plexus cannot be definitely set out, owing to their variability, within the frame of a definite scheme (Hovelacque); as a rule they originate from the stellate ganglion or from the second and third thoracic ganglia. These vagus-sympathetic anastomoses among cardial nerves of the two systems have a great importance, for through them the lung is reached by a considerable complex of sympathetic fibers going in a small portion to the anterior pulmonary plexus. The larger and more conspicuous group of pulmonary nerves detaches itself from the vagus in the section where the latter crosses the posterior part of the bronchus. From these nerves originate capillary branches, partly innervating the bronchus and partly innervating the pulmonary parenchyma and the vessels. The above branches, which have been described as belonging to the vagus, contain a sympathetic component proceeding from vagosympathetic anastomoses of the upper portion of the thorax. The bronchopulmonary branches properly anastomosed constitute the posterior pulmonary plexus and are particularly laid in proximity of the reflection line of the mediastinal pleura on the lung root; while extending toward the hilus, a few fibers pass over the bronchus, placing themselves on its ventral aspect. Thus, the bronchus, in its segment close to the pulmonary hilus, is mainly covered by bronchopulmonary nerve ramifications. On the posterior aspect of the root run the bronchial arteries accompanied by their nervous equipment, the filaments of which extensively anastomose themselves with those of the vagus. In the left portion of the hemithorax the nerve distribution and topography are mainly similar to those of the right hemithorax. It is, however, important to lay stress on the fact that, as already demonstrated by Taft, the pneumocardial branches of the left hemithorax split themselves at a higher level and are surrounded by loose connective tissue, without establishing a too close connection with the vessels and the bronchi, while on the right side the same are rather close to the trachea. At a later stage Taft gave much importance to this anatomic display in order to explain the greater danger of pulls on the right pulmonary root noticed by Sauerbruch, Graham, and by Denk in human surgery, and experimentally demonstrated by Kusakabe. The latter, by electric stimulation of the right pulmonary root of a dog, noticed a more distinct slackening of pulsation and respiration together with a lowering of blood pressure than by stimulating the left pulmonary root.

From the foregoing brief anatomic premises it follows that the functions of the cardiac and pulmonary vagus are likely to be reciprocally influenced.

The cooling of these nerves at the neck causes, indeed, a cardiac acceleration reflecting itself in respiratory changes; likewise, the electric stimulation of the central trunk of the vagus causes respiratory and pressure changes proportionate to the concentration and the duration of the stimulations.

Stimulations of weak concentration produce an increase of respiration frequency and a decrease in the size of the thorax when in an inflationary position; an increase in stimulating power still increases these effects; when the frequency and the intensity become greater, respiration stops in an inflation position which may be turned into a deflation position through stimulations of a still greater intensity.

The effects on pressure are even more changeable: light stimulations produce at first a lowering of pressure (Hunt); increased stimulation decreases depressing effect; much stronger stimulation increases pressure proportionate to its frequency and duration. When the increase of pressure is not very strong, the interruption of stimulation produces a decrease of pressure and a respiratory acceleration.

The pressure effect of stimulation may be transformed into a contrary effect by the action of anesthetics (Cyon) or by the cooling of the nerve (Hunt).

The reason for this variable response has been attributed to the presence of stimulating and depressing fibers both in the vagus (Heymans, Mac Oswallo, Tournade) and the other sensory nerves (Hunt).

Cannon and Rapport attribute the lowering of pressure to reflex inhibition of adrenalin secretion (adrenergic-sympathetic fibers).

Though the functions of the sympathetic nerve are known in their broad lines, they are still scarcely known in their mechanical reflexogenic endothoracic details.

Though attributing to the vagus and the sympathetic nerves the greatest importance in the determination of reflexes on blood pressure and respiration, one should pay particular attention to the diaphragmatic receptors sending their impulses to the center and to the periphery by way of the phrenic nerve.

In natural respiration there are discharges of impulses synchronizing with inflation and proportionately larger as respiration becomes more energetic. In apnea caused by hyperventilation the nerve rests but becomes active again when aspiration is made in the trachea or when the abdomen is so compressed as to push the diaphragm toward the thorax (Cardin).

Discharges of impulses are caused even when a pull in cephalic direction is made on the tendinous center of the animal's diaphragm when the thorax has been opened (Cardin). In respect of tension, of change of circulatory and respiratory conditions, and of blood gases, these diaphragmatic tensorceptors behave in exactly a similar way as the tension propioceptors of the pulmonary vessel (Adrian) and of the carotid sinus (Matthew and Brouk). It is generally admitted that the rhythm and the depth of respiration are governed by nervous impulses coming from the lung (Hering-Breuer) and reaching the respiratory center through the vagus (Adrian).

Electric stimulations of the afferent discharges directed toward the center from the pulmonary fibers of the vagus show that during normal respiration rhythmical impulses are determined only during inflation, and the impulse frequency in each single fiber is in relation to the entity of distention of the lung and is not liable to large variations until that particular stimulation lasts. By varying the stimulation, respiratory modifications can be favored and be made to influence blood pressure. This shows that pulmonary receptors are not liable to a prompt adaptation, yet in tracheotomized animals balancing and adaptation reflexes have been noticed to set in, in order to re-establish a proper pressure balance.

Head, Hommonda, and Wilson explain such balancing reflexes by admitting the presence of a further order of afferent fibers interested in Hering-Breuer reflexes. Such fibers displayed their action more especially during pulmonary collapse, as was demonstrated during experiments made by extracting air from the lung, and also during a respiratory spasm in order to compensate for an obstruction (Whitteridge). It seems that the coordinated activity of these two fiber systems regulates the rhythm of respiration, thus harmonizing the inflation and deflation mechanism.

Surgical experience past and present shows that thoracotomy by itself, pleural, endothoracic, pericardial, and diaphragmatic stimulation, may cause hypotensive reflexes, but it is commonly agreed today that such reflexes mainly originate by direct stimulation of the hilus and the pulmonary root. In these hilar areas surgeons endeavor to attenuate the vagal-sympathetic tonus by using Novocain infiltrations of the pulmonary hilus and its elements.

O'Shaughnessy observed that respiratory alterations particularly follow faradic stimulation of the posterior pulmonary root, owing to the reflexes generated in the posterior pulmonary plexus unusually rich in centripetal vagal branches belonging to the bronchial nervous system. By stimulating the anterior aspect of the root, and more especially the pulmonary veins, O'Shaughnessy noticed a modification of the cardiac rhythm and a fall of blood pressure. This author believes that fibers running near the pulmonary veins originate in the deep cardiac plexus and have no connection with the vagus trunk. In conclusion, the fall of pressure would be due to a local reflex following direct irritation of the nerve center of the heart.

According to Bross and Lueken pressure falls are particularly due to the bronchoconstrictive action of the vagus.

Bilfeldt-Nicholls and Escala Bawden (1946) give much importance to mediastinal fluctuation and to mechanical impediment of the blood flow into the heart in order to explain the origin of the serious hypotensive reflexes. Morin and Dei Poli believe that a portion of reflexes capable of producing more noticeable changes of blood pressure are exclusively due to stimulation and pulling of the pulmonary veins; they attach great importance to the sensitive receptors of the subendothelial stratum of the pulmonary veins.

The researches made by these authors justify the necessity of Novocain infiltration of the hilus and of the pulmonary root.

Today, with controlled respiration narcosis, it is possible to harmonize, even with a wide-open thorax, pulmonary rhythm and thus eliminate a portion of the causes likely to discharge hypotensive reflexes caused by sudden modifications of pulmonary ventilation.

With the use of curare, relaxation of the respiratory and intercostal muscles, and even of the diaphragm, can be obtained if so required. Yet even by this technique vagal and diaphragmatic depressive reflexes are not abolished.

In March, 1947, Parenti submitted to the Societa' Piemontese di Chirurgia the favorable results obtained by him in thoracic surgery during World War II by a simultaneous anesthesia of the vagus, of the sympathetic, and of the phrenic at the neck. According to him, by this anesthesia pleural shock, respiratory collapse, and cough are attenuated, while operating conditions and those of the patient are improved.

Starting from Parenti's observations, I made the object of my researches not merely to check the practical advantage of his suggestion, but also to verify whether by this technique it is possible to attenuate hypotensive reflexes not merely arising from the pleura, as in accordance with the author's premises, but originating above all by surgical maneuvers of the hilus and of the pulmonary root.

Such reflexes are particularly dangerous in vagotonic subjects and cannot be completely suppressed by Novocain infiltrations in the pulmonary hilus (Soave). In everyday practice, while anesthesia of the sympathetic and alcoholization of the phrenic are used for therapeutic aims, it does not appear that the simultaneous anesthesia of the three nerves (vagus, sympathetic, and phrenic) as studied by me has yet been applied.

TECHNIQUE

The experiments were made on twenty dogs of robust constitution duly anesthetized with a solution of chloralose, 5 ctg. every kilogram weight, and urethane, 35 ctg. every kilogram weight, administered by intravenous injections, the operating room being kept at a constant temperature, pressure, and moisture. Blood pressure during the whole experiment was registered by connecting a Ludwig manometer to the femoral artery. Time spent on the operation was registered by a tonometer. Magnesium sulfate was used to prevent clots from obstructing blood pressure readings.

Each animal, after general anesthesia, was submitted to artificial respiration by way of a Palmer pump and the chest cavity was subsequently opened after the removal of a rib. All experiments were made on the right hemithorax for the reasons just mentioned.

Through the lateral opening and using a curved Klemmer with long and thin tongues I have carried out a number of mechanical compressions and pulls of the lung root in its entirety, of the lung veins, and of the pulmonary artery alone. Such mechanical compressions, stimulations, and pulls have been exerted in all animals before and after anesthetic block of the three nerves (vagus, sympathetic, and phrenic) at the neck.

The injection was made with a very thin needle, using a 0.50 per cent solution of Novocain, without adrenalin, in doses of 10 to 20 c.c. After having pulled aside with a finger the middle margin of the sternocleidomastoid, the same finger was used to shift the common carotid and the exterior jugular vein. By this maneuver the vagus, which lies at the top corner formed by these two vessels, is also shifted and has a tendency to superimpose itself on the sympathetic cord. Having thus externally deviated the vessel bundle and always keeping the vessels well aside, the needle is deeply inserted until it reaches the stratum of the deep neck muscles, and in this area (lower margin of the larynx) the anesthetic infiltration is applied.

It is thus possible to obtain vagus and sympathetic anesthesia. In order to reach the phrenic one must push forward the needle point for approximately ¼ cm. Then, sliding on the prevertebral fascia above the anterior scalene, the needle is in the immediate vicinity of the phrenic.

The complete protocols of the experiments carried out by the author are not given here. Only diagrams of some experiments are reported.

The experiments carried out by me have confirmed that:

(1) In normal animals crushing of the lung root in its entirety causes a considerable drop of blood pressure which becomes accentuated if stimulation is made by pulling.

(2) Crushing of pulmonary veins is followed by a drop of blood pressure considerably lower than that caused by the crushing of the entire root. If lateral or inferior stimulation by pulling is added to vein crushing, a more pronounced blood pressure takes place.

(3) Crushing and pulling of the pulmonary arterial branch causes less pronounced alterations of blood pressure.

The hypotensive reflexes caused by surgical maneuvers have generally been proved to be reversible, and the level of blood pressure has been established in a more or less constant lapse of time (in seconds) for all animals.

In all animals treated with the simultaneous block of the vagus, the sympathetic, and the phrenic at the neck under the same experimental conditions, I have constantly noticed that hypotensive reflexes were always present, but much less pronounced and more rapidly reversible.

The aim of my study was to establish, through a scientific demonstration, whether this anesthetic block attenuates, better than Novocain infiltration of the root, the alterations of blood pressure caused by manipulations of pulling or crushing of the lung root after the chest cavity has been opened.

I believe that the block at the neck, by inhibiting a large portion of the phrenic, eliminates the diaphragm's spasm and diminishes reflexes originating in diaphragmatic tensoreceptors which trouble blood pressure; in the second instance it is likely that simultaneous anesthetic action of the vagus and the sympathetic may considerably mitigate reflexes proceeding from the root. It is easy to notice this in Figs. I to VII. I have always exerted the pulling in such a way as not to cause a shifting of the mediastinum, in order to avoid the production of hypotensive reflexes due to the indirect pull of the nervous plexi of the hemithorax.

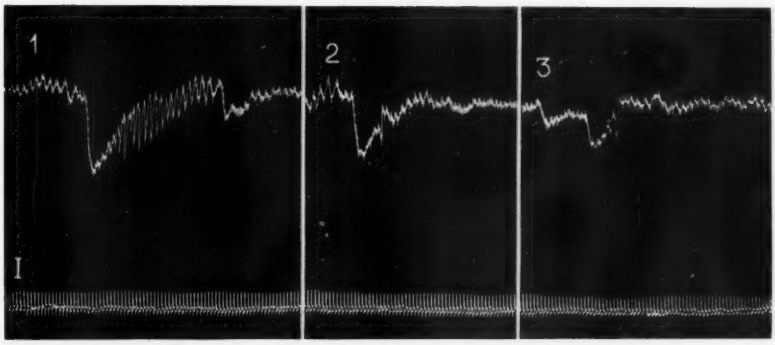

Fig. I (Experiment 1, Trial 1, Control).—*1*, Crushing and pulling of lung root in its entirety; *2*, similar maneuver on pulmonary veins; *3*, similar maneuver on pulmonary artery. (Figs. I to VII from Chirugia, Milano, No. 5-6 1948.)

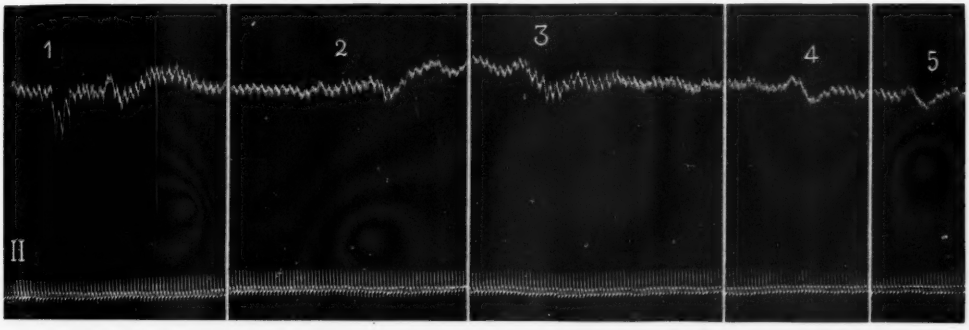

Fig. II (Experiment 1, Trial 2).—After twenty minutes from the previous trial the block of the three nerves is exerted at the neck. *1*, Crushing of the root; *2*, crushing of the bronchus; *3*, after ten minutes, crushing of pulmonary veins; *4*, crushing of pulmonary artery; *5*, crushing and pulling of the bronchus.

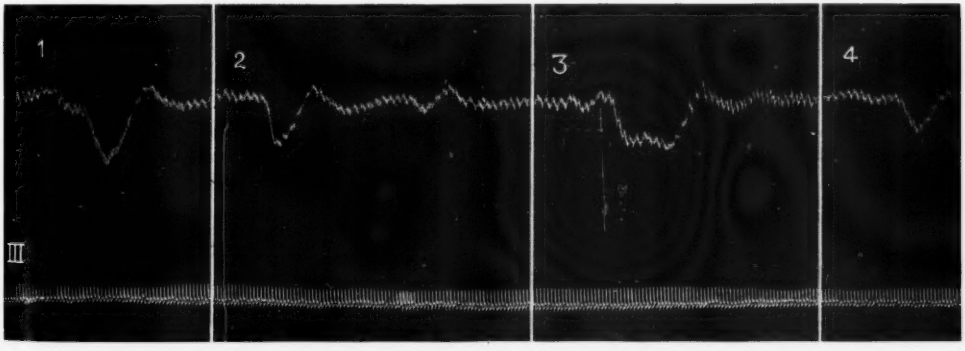

Fig. III (Experiment 2, Trial 1, Control).—*1*, Crushing and pulling of lung root; *2*, after ten minutes, crushing of pulmonary veins; *3*, crushing and pulling of pulmonary veins; *4*, after ten minutes crushing and pulling of pulmonary artery.

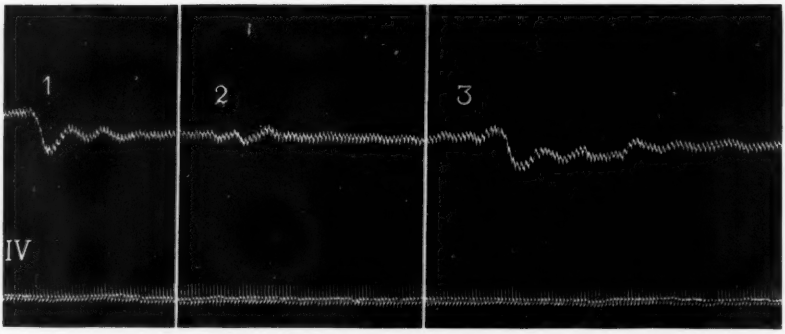

Fig. IV (Experiment 2, Trial 2).—After twenty minutes from the first trial, the blocking of the three nerves is exerted. *1*, Crushing and pulling of root; *2*, crushing and pulling of pulmonary artery; *3*, crushing and pulling of pulmonary veins.

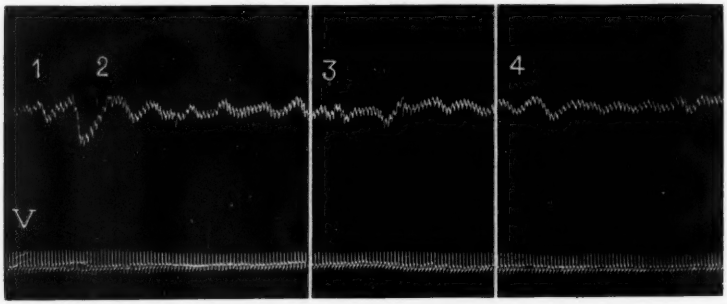

Fig. V (Experiment 3, Trial 2).—After twenty minutes from Trial 1 the blocking of the three nerves is exerted. *1*, Crushing of pulmonary veins; *2*, crushing and pulling of pulmonary veins; *3*, crushing of pulmonary artery; *4*, crushing and pulling of pulmonary artery.

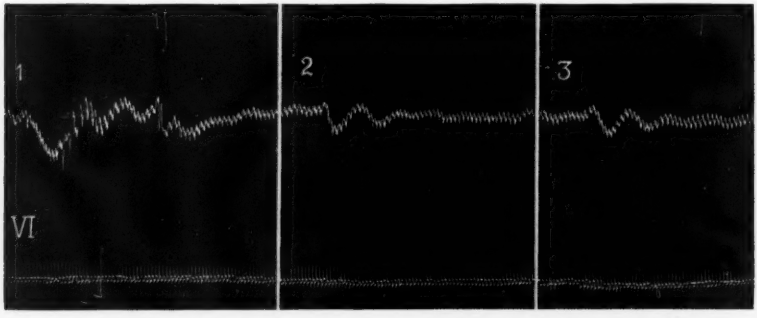

Fig. VI (Experiment 4, Trial 2).—After thirty minutes from the first trial the blocking of the three nerves is exerted. *1*, Crushing and pulling of root: *2*, crushing and pulling of pulmonary artery; *3*, after ten minutes, crushing of the pulmonary veins.

When I further consider the relative difference of hypertension caused by the crushing and the pulling of pulmonary veins and I compare it with the drop of blood pressure caused by equal stimulations exerted on the complete lung root (which is only slightly more noticeable), I must admit with O'Shaughnessy, Morin, and Dei Poli that the most noticeable cardiocirculation reflexes mainly originate from the stimulation of the nervous perivenous component and more especially subendothelial, owing to the presence of pressure receptors similar to those of the carotid sinus and of the aortic cardioreceptor area.

In a general way I can conclude that by the anesthetic blocking of the vagus, the sympathetic, and the phrenic at the neck, depressing cardiocirculatory reflexes are considerably attenuated but not abolished.

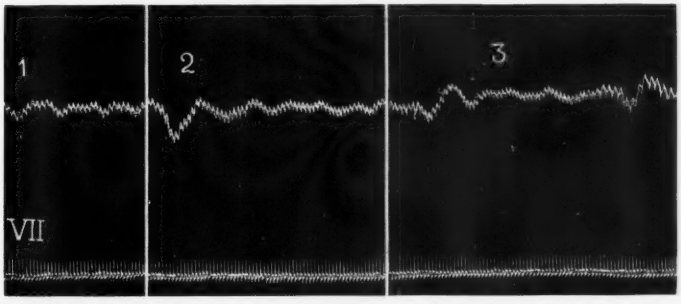

Fig. VII (Experiment 5, Trial 2).—Twenty minutes after the first trial the blocking of the three nerves is exerted. *1*, Crushing of the pulmonary artery; *2*, crushing and pulling of the pulmonary veins; *3*, crushing and pulling of pulmonary artery.

In a general way, by the simultaneous anesthesia of the three nerves, it would be possible to achieve in thoracic surgery what has been achieved in abdominal surgery through the anesthetic protection of the splanchnic, that is, a less marked drop of blood pressure when a pull of visceral pedicles is exerted.

SUMMARY

After having briefly recalled that thoracic surgery largely owes its marvelous development to narcosis improvements, the author examines the possible site of origin of hypotensive reflexes during pneumonectomies and lobectomies. With a practical aim in view he has experimentally studied artificial respiration on dogs previously narcotized and the action of blood pressure with and without neck anesthesia of the vagus, sympathetic, and phrenic. The object of his research was to establish whether this type of anesthesia, added to general or peripheral narcosis, cannot only eliminate pleural reflexes (Parenti) but also attenuate hypotensive reflexes arising from stimulation, crushing, and pulling of the pulmonary root in its entirety and of its components. The author concludes in favor of his researches and advises the use of this subsidiary therapy in general thoracic surgery.

This study was done at the Surgical Department of the University of Torino, Professor A. M. Dogliotti, director.

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NOTICE

In June, 1949, the Secretary of the Board of Thoracic Surgery met with the American Board of Surgery, and the problem of those individuals who are neither members of The American Association for Thoracic Surgery nor diplomates of the American Board of Surgery was considered. The American Board of Surgery allowed a new group to be admitted to the Founders Group at the discretion of the Board of Thoracic Surgery. This group will be known as group "D" and will consist of other surgeons who are not members of The American Association for Thoracic Surgery or diplomates of the American Board of Surgery and whose training, because of the period in which it was taken, does not qualify them to become certified by the American Board of Surgery, but who may upon careful scrutiny and adequate evidence of proficiency be eligible for consideration as founder members.